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The American Heart Journal

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The American Heart Journal

VOL. II JUNE, 1927 No. 5

Original Communications

THE INFLUENCE OF CHANGES IN THE CARDIAC RATE AND IRREGULAR ACTION OF THE HEART ON THE CORONARY CIRCULATION*

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THE slow cardiac rate associated with complete heart-block and the accelerated rate accompanying auricular fibrillation, flutter, and paroxysmal tachycardia are known to reduce the efficiency of the heart. It occurred to us that possibly the response of the heart to these conditions may, in part, be due to their influence on the coronary circulation. In the present investigation the rate of the coronary flow was studied with reference to the effects produced by changes in heart rate and by the induction of cardiac irregularities.

The influence of cardiac rate on the coronary flow has been studied experimentally, but there is considerable disagreement in results obtained. Porter[1] noted a decrease in the rate of flow of the perfusate through the coronary arteries of the cat when the heart rate was slowed by vagal stimulation. He concluded that the volume of blood passing through the coronary arteries was influenced by the cardiac rate. Wiggers[2] has called attention to the influence of the rate and force of contractions on the coronary circulation and attributes this effect to the massaging action of the cardiac musculature.

Nakagawa[3] employing the heart-lung preparation and Sassa[4] in studies on the isolated heart produced changes in the rate by altering the temperature of the blood or the perfusion fluid. The results in the two series of experiments were similar. The reduction and acceleration in the cardiac rate induced respectively by cooling and heating the blood or perfusing fluid produced an increase and decrease in the rate of coronary flow. These investigators appreciated that the changes

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Read before The American Physiological Society at Rochester, New York, April 15, 1927.

in the coronary flow induced in this manner could not be entirely attributed to changes in the cardiac rate. They then resorted to other means of changing the cardiac rate. Nakagawa, in his further experiments, slowed the heart by vagal stimulation and accelerated the rate by induced shocks to the sinus node. In neither instance was any appreciable change observed in the rate of the coronary circulation. Sassa, in his subsequent studies, produced changes in the cardiac rate by cooling and warming the sinus node by means of a water thermode. He observed a decrease in the rate of coronary flow when the cardiac rate was reduced. When, however, the cardiac rate was accelerated by the application of heat to the sinus node there was no significant increase in the rate of flow through the coronary arteries.

Morawitz and Zahn[5] studied the influence of heating and cooling of the sinus node on the coronary circulation. In their experiments, however, a uniform blood pressure was not maintained.

TABLE I

	INCREASE IN HEART RATE (BEATS PER MINUTE)	INCREASE IN CORONARY FLOW PER CENT
	from 124 to 160	1.0
Experiment I	" 120 " 176	28.0
	" 120 " 200	25.0
	" 132 " 160	2.4
Experiment II	" 132 " 168	10.5
	" 132 " 176	10.5
	" 128 " 200	13.0
Experiment III	" 128 " 212	8.0
	" 128 " 224	13.0
	" 176 " 188	4.5
Experiment IV	" 176 " 196	4.5
	" 176 " 212	16.5
	" 176 " 212	8.0
Experiment V	" 176 " 224	5.3
	" 176 " 236	3.7

More recently Hammouda and Kinosita[6] and also Anrep and Segall,[7] working with the isolated heart and with the heart-lung preparation, observed no change in the rate of the coronary circulation when the heart was driven at varying rates.

In the present investigation the effect of changes in the cardiac rate on the coronary circulation was studied both on the isolated heart and on the heart in situ. In the former the heart of the rabbit was driven at different rates by means of rhythmically induced shocks. In every instance an increase in the cardiac rate was associated with an augmentation of the coronary flow (Table I). It is to be noted that the greatest increase in the rate of the coronary circulation was obtained in those experiments in which the initial cardiac rate was approximately

120 per minute and the acceleration was at least 50 beats per minute. When, however, the initial heart rate was above 150 beats per minute, the acceleration was not accompanied by an increase in the coronary circulation comparable to that obtained in experiments with a lower initial cardiac rate.

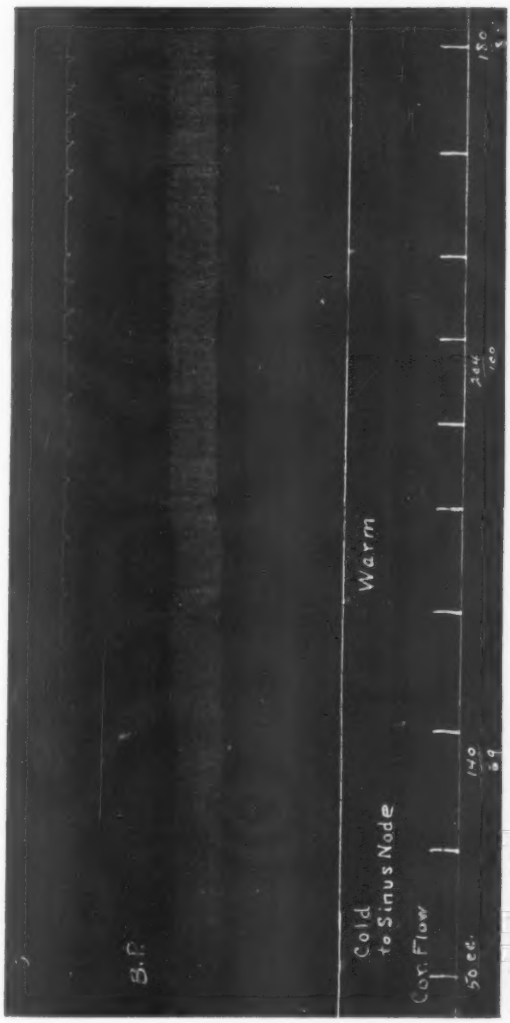

Fig. 1.—Cardiac rate altered by cooling and warming the sinus node. During the cooling of the sinus node the cardiac rate was 140 per minute, and the coronary flow, 69 c.c. per minute. On warming the sinus node the cardiac rate was 204, and the coronary flow, 100 c.c. On stopping the application of heat, the cardiac rate was 180, and the coronary flow, 85 c.c.

Further studies were made on the intact heart of the dog. The rate of coronary circulation was studied by means of the Morawitz-Zahn cannula. A constant blood pressure was maintained by reintroducing the blood from the coronary sinus into a femoral vein at a uniform rate. Blood pressure was recorded by a Straub membrane manometer. Changes in cardiac rate were induced by heating and cooling the sinus

node and by vagal stimulation. In the heating and cooling experiments, the changes in the temperature of the sinus node were produced by the application of a small thin rubber bag containing warm or cold

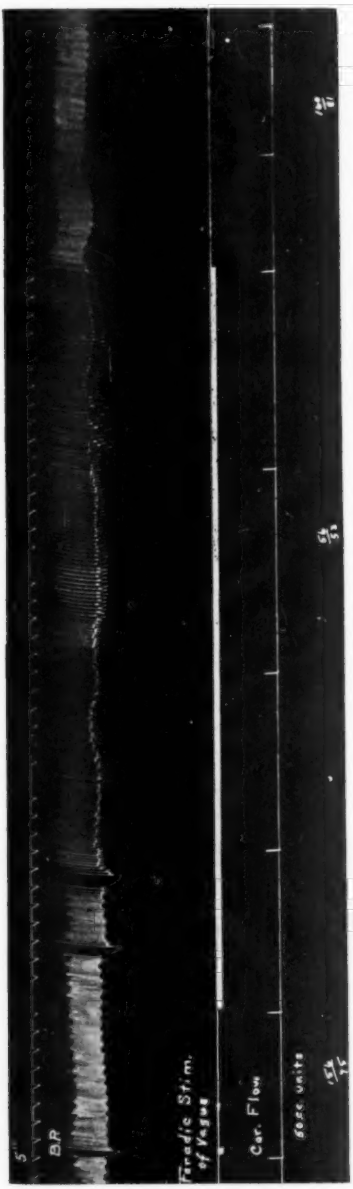

Fig. 2.—Progressively increasing stimulation of the vagus nerve. During the control period, the cardiac rate was 156 per minute, and the coronary flow, 75 c.c. per minute. During the period of slowing, produced by progressively increasing the strength of vagus stimulation, the mean cardiac rate was 56, and the mean coronary flow, 53 c.c. After discontinuing vagal stimulation, the cardiac rate was 160, and the coronary flow, 81 c.c.

water. The application was limited as closely as possible to the sinus node. A greater range in the cardiac rate was obtained by changing immediately from the cold to the warm applications. By this method

it was possible to produce changes in the cardiac rate ranging from 30 to 60 beats per minute.

Changes from cold to warm were always accompanied by an increase in the rate of coronary circulation. In Fig. 1 an experiment is shown in which the cardiac rate was 140 per minute during the application of cold to the sinus node, and the rate of flow from the coronary sinus was 69 c.c. per minute. Following the application of heat, the cardiac rate was accelerated to 204 per minute, and the flow from the coronary sinus increased to 100 c.c. per minute. In other experiments in which this means of changing the cardiac rate was employed, the results were similar. In those experiments in which the cardiac rate was reduced by vagal stimulation, there was a striking decrease in the rate of the coronary circulation. In Fig. 2 the initial cardiac rate was 152 per minute and the flow from the coronary sinus 75 c.c. per minute. A gradually increasing strength of stimulus was used. It is to be noted that there was a gradual reduction of the cardiac rate during the period of vagal stimulation, associated with a progressive decrease in the rate of flow from the coronary sinus. The approximate mean cardiac rate induced by vagal stimulation was 56 beats per minute and the flow from the coronary sinus 53 c.c. per minute. After the vagal stimulation was discontinued, the cardiac rate increased to 160 beats per minute, and the flow from the coronary sinus rose to 81 c.c. per minute. In another experiment (Fig. 3) greater extremes in the cardiac rate were produced by the application of heat to the sinus node as soon as vagal stimulation was discontinued. The decrease in cardiac rate was associated with a 20 per cent reduction in the rate of flow from the coronary sinus, despite a marked elevation of the systolic blood pressure.

The reduction in rate of coronary circulation induced by vagal stimulation is attributed to the decrease in cardiac rate. We have, in numerous experiments, stimulated the vagus nerve of the dog, while a constant cardiac rate was maintained by rhythmically induced break shocks, and never have we observed any appreciable decrease in the rate of coronary circulation.

It would seem that the results relative to the influence of change in cardiac rate on the coronary circulation in both the isolated and the intact heart are in general accord. A reduction or an acceleration of the heart rate is, within certain limits, associated with a decrease or an increase in the rate of coronary circulation. The most striking change in the coronary circulation was obtained in those instances in which relatively great changes in cardiac rate were produced. This was possible in the experiments with the isolated heart where the initial rate was relatively slow, and in the intact heart by the use of vagal stimulation. It is our feeling, however, that the heart cannot be progressively accelerated to extremely high rates and this change still

be accompanied by an increase in the rate of the coronary circulation. In our experiments this extreme degree of acceleration was not employed, but we observed, with the higher rates at which the heart was

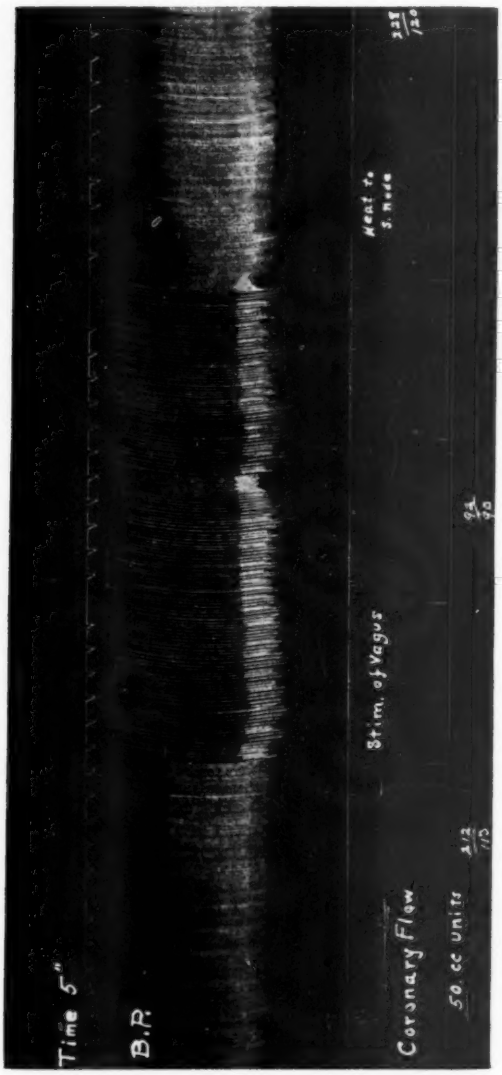

Fig. 3.—Intermittent stimulation of vagus nerve. During the control period, the cardiac rate was 212, and the coronary flow, 113 c.c. During vagal stimulation the cardiac rate was 92, and the coronary flow, 90 c.c. During application of heat to sinus node, the cardiac rate was 228, and the coronary flow, 120 c.c.

driven, that the increase in the rate of coronary circulation was not comparable to the cardiac acceleration. It is not improbable that this factor may contribute to the reduction of the efficiency of the heart in

clinical conditions accompanied by excessive cardiac rates, even though a constant blood pressure is maintained. If, in addition, there is an associated decrease in the blood pressure there would no doubt be a further reduction in the rate of coronary circulation.

We have found little in the literature concerning the blood pressure in paroxysmal tachycardia. Hirschfelder[8] states that the blood pressure frequently falls in paroxysmal tachycardia. He cites one instance in which, prior to an attack, the systolic pressure ranged from 165 to 190 and the diastolic from 100 to 115, whereas, during the paroxysms, the maximum systolic pressure was 130 and the diastolic 95 to 100. Willius, in a personal communication, states that he has noted a marked reduction in both the systolic and the diastolic pressure following the onset of paroxysmal tachycardia. He mentioned one patient in whom the systolic pressure was 190 and the diastolic 115 when the cardiac rhythm was normal. During an attack, however, in which the cardiac rate was 200 per minute, the systolic pressure dropped to 95 and the diastolic to 85. He further states that similar blood pressure readings have been obtained in other patients with paroxysmal tachycardia. Under these circumstances there would, no doubt, be a marked reduction in rate of coronary circulation due to the low blood pressure and, in part, to the excessive cardiac rate.

In our experiments with very slow cardiac rates, the volume of the coronary circulation was reduced 20 to 30 per cent below that observed during the control period. It would seem that a similar reduction might occur in complete block of the auriculoventricular bundle.

IRREGULAR ACTION OF THE HEART

Anrep[9] in a recent review has referred to work which is still in press on the influence of heart-block, premature contractions, auricular and ventricular fibrillation on the time relation between the changes in the coronary inflow and outflow and the different phases of the cardiac cycle. There have been no other experiments, to our knowledge, concerning the effects of the clinical types of cardiac irregularities on the coronary circulation.

In this part of our study, observations were made on the heart of the dog in situ. The rate of the coronary circulation was determined by means of the Morawitz-Zahn cannula. Premature contractions were produced by stimulating the auricles or the ventricles with single, induced, break shocks. Auricular fibrillation was induced by faradic stimulation of the auricle. It was recognized that the electrical stimulation of the heart might, in itself, influence the coronary circulation. An attempt was thus made to induce the auricular fibrillation with a minimum faradic stimulation. The stimulation was discontinued as soon as we were certain that the induced cardiac mechanism would persist.

The production of premature contractions in rapid succession, re-

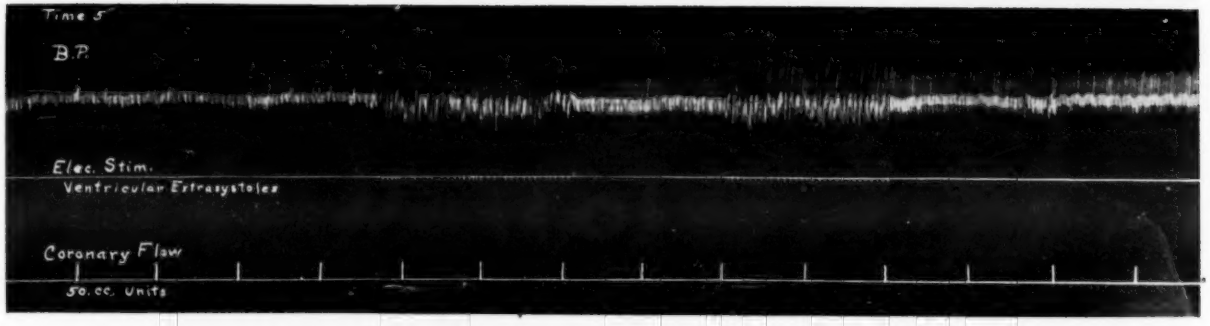

Fig. 4.—Ventricular extrasystoles. No change in coronary flow.

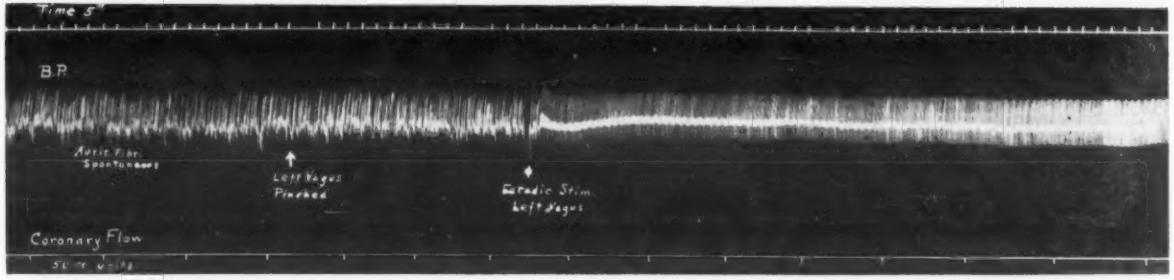

Fig. 5.—Spontaneous auricular fibrillation. Cardiac rate was 224 (many beats inefficient); coronary flow was 109 c.c. per minute. After establishing normal rhythm by brief stimulation of vagus, the cardiac rate was 160, and the coronary flow, 100 c.c. per minute.

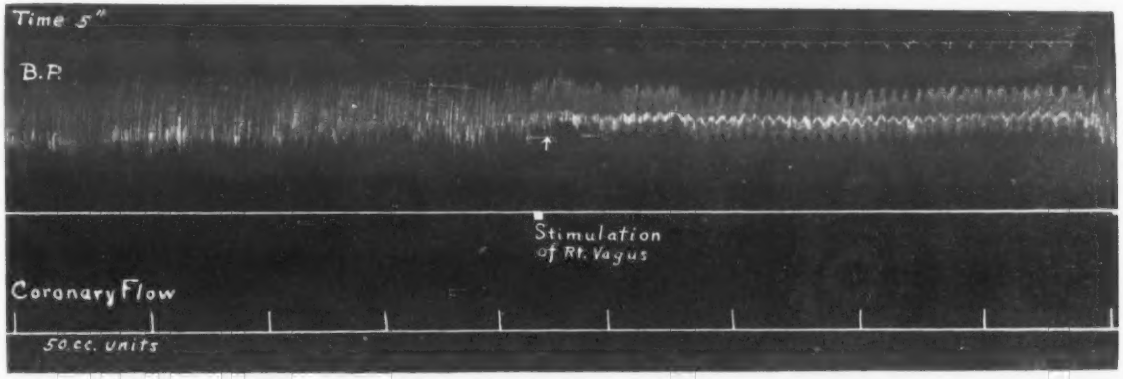

Fig. 6.—Induced auricular fribrillation. Cardiac rate was 216 (many beats inefficient); coronary flow, 109 c.c. After establishing normal rhythm, the cardiac rate was 164, and the coronary flow, 100 c.c.

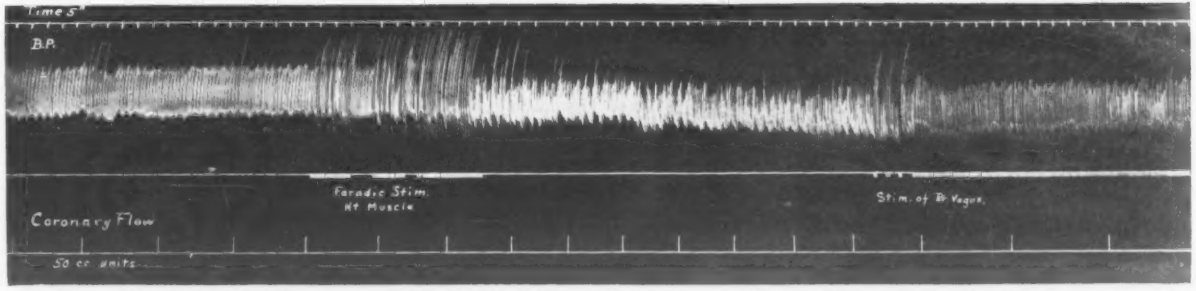

Fig. 7.—Induced rapid heart action. During the control period, the cardiac rate was 172, and the coronary flow, 125 c.c. During induced rapid heart action, the cardiac rate was 280, and the coronary flow, 162 c.c. During stimulation of vagus, the cardiac rate was 116, and the coronary flow, 97 c.c.

gardless of whether they originated in the auricle or in the ventricle, did not have any significant influence on the coronary circulation. A tracing from such an experiment is shown in Fig. 4.

The results of faradic stimulation of the auricles varied in regard to the cardiac mechanism produced. In some instances a very fine fibrillary contraction of the auricles followed, which was associated with a grossly irregular action of the ventricles. In other experiments the auricular contractions were larger, more uniform, and were accompanied by very rapid and more regular ventricular contractions. The onset of auricular fibrillation was frequently associated with a reduction in the blood pressure. It was, however, possible to maintain a fairly constant pressure by reintroducing the blood into the femoral vein at a more rapid rate.

The rate of the coronary circulation was either not appreciably influenced or was moderately accelerated by the induction of auricular fibrillation. In the experiment shown in Fig. 5, auricular fibrillation appeared spontaneously and lasted until interrupted by stimulating the vagus.

It is to be noted that there is no appreciable change in the rate of flow from the coronary sinus following the establishment of normal rhythm. The results were similar in other experiments. In Fig. 6 auricular fibrillation was easily induced by faradic stimulation of the auricular muscle and the normal mechanism was reestablished by a brief stimulation of the vagus. The carotid pulse rate during the auricular fibrillation was estimated to be 216 per minute (many contractions were very inefficient), while the flow from the coronary sinus was 109 c.c. per minute. After the return to normal rhythm, the carotid pulse rate was reduced to 164 beats per minute and the flow from the coronary sinus, to 100 c.c. per minute. In another experiment, illustrated by Fig. 7, the carotid pulse rate, following the induction of auricular fibrillation, was increased from 172 to 280 per minute and the flow from the coronary sinus from 125 to 162 c.c. per minute.

These results seem to indicate that the volume of the coronary circulation, in experimentally produced auricular fibrillation, varies with the rate and the strength of the ventricular contractions. It is appreciated that the true ventricular rate is not shown in the blood pressure curves during auricular fibrillation. It is evident, however, that there is a greater acceleration of the carotid pulse rate, and that the ventricular contractions as indicated by the membrane manometer are more uniform in Fig. 7 than in Figs. 5 and 6. There are consequently a greater number of efficient ventricular contractions per unit of time in the former than in the latter instances. Since the increase in coronary flow occurred without an increase in blood pressure, we feel that it can reasonably be explained on the basis of the increased rate and regularity of ventricular action. It would thus seem that the rate of the

coronary circulation in auricular fibrillation is, within certain limits, dependent upon the rate and force of the ventricular contractions, if blood pressure remains constant. The results further suggest that in clinical auricular fibrillation, particularly where the pulse deficit is great, the extra work imposed by the absolute irregularity is out of proportion to any increase in the rate of the coronary circulation. If in clinical auricular fibrillation the blood pressure be decreased, this fall in blood pressure would likely become the dominant factor in determining the change in coronary circulation.

SUMMARY

A reduction and an acceleration of the cardiac rate were, within certain limits, associated with a decrease and an increase in the rate of the coronary circulation. The most striking changes in the rate of the coronary flow were observed in those instances in which relatively great changes in cardiac rate were induced. It is suggested, however, that a heart cannot be progressively accelerated to extreme degrees with an accompanying increase in the coronary circulation.

In the very slow cardiac rates induced by vagal stimulation, the rate of flow from the coronary sinus was reduced from 20 to 30 per cent below that observed during the control period.

The production of auricular or ventricular premature contractions did not have any significant effect on the rate of flow from the coronary sinus.

In auricular fibrillation, the rate of the coronary circulation either remained fairly constant or was moderately accelerated. The results seemed to depend on the rate and the force of the ventricular contractions associated with the absolute irregularity.

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CARDIAC PAIN IN PAROXYSMAL TACHYCARDIA*

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IT IS sometimes difficult to make a diagnosis of angina pectoris. Inasmuch as physical signs of cardiac disease may be absent and electrocardiographic data negative, there are times when the diagnosis must rest entirely on the subjective history elicited from the patient. From time to time patients are observed who complain of pain which closely simulates the syndrome originally described by Heberden, and which requires an explanation on a basis other than that of angina pectoris of primary cardiac disease. A better understanding of the mechanism of the production of cardiac pain clarifies the diagnosis and furnishes a rational basis for the existence of the pain in a certain group of cases.

From a group of 380 cases in which a diagnosis of paroxysmal tachycardia was made, nineteen (5 per cent) were selected to form the basis of this study. Eleven of the patients were females and eight were males. The average age of the males was forty-eight years and all except two were more than forty-four. The average age of the females was forty-five years; three were less than thirty.

The blood pressure readings were above normal in seven cases, normal in eleven, and not recorded in one. The highest systolic pressure recorded was 200 mm., and the highest diastolic 120 mm. Only one of the patients with normal blood pressure had objective evidence of cardiac disease. This patient presented the classic symptoms of chronic rheumatic endocarditis with mitral stenosis and insufficiency. Only three of the patients with blood pressure above normal had objective evidence of cardiac disease. One presented evidence of aortic sclerosis, one of aortic sclerosis and moderate cardiac hypertrophy, and the third of cardiac hypertrophy alone. Only one patient showed signs of cardiac failure during the attacks of paroxysmal tachycardia. Except that seven patients had foci of infection, there were no data to signify other pathological conditions in this group of patients.

Electrocardiograms of eighteen patients were made either in the interval between attacks or during a paroxysm of rapid heart action. Electrocardiograms were made of thirteen cases in the interval between

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attacks; the tracings did not reveal significant abnormalities. Tracings were taken of four cases during attacks; one showed ventricular tachycardia with a rate of 169, one auricular flutter and a rate of 214 with a 1:1 auriculoventricular ratio, one nodal tachycardia with a rate of 200, and one nodal tachycardia with a rate of 196. One case of hypertension and arteriosclerosis showed T-wave negativity in Lead I. It was not possible to obtain tracings in two cases which were observed during typical attacks of paroxysmal tachycardia.

The length of time the patients had been subject to attacks of paroxysmal tachycardia varied from two weeks to twenty-two years, the average being ten years; in some cases pain did not appear for several years. The average length of time in which there was pain during attacks was eight and a half years.

As a rule the patients described the pain as aching in character. One patient described a sense of oppression in the epigastrium, one had experienced a sense of constriction over the precordial region, and one had had lancinating pains. Four patients feared impending death during the painful seizures.

In ten cases the pain was precordial, with radiation into the left shoulder or left arm in seven. Moderate to severe dyspnea was present during attacks in three cases. In eight cases the pain was referred to the sternal area with a greater tendency to radiate into both arms and shoulders than in cases in which the pain was precordial. In one case the pain was in the epigastrium and in another in the back, synchronous with the substernal pain. In one atypical case the paroxysm of tachycardia was associated with a sense of epigastric oppression and with pain which extended up to the lower sternal and apical regions.

In contrast to angina pectoris, in only one case of this group was exertion held responsible for the paroxysmal tachycardia and the attack of pain. In general, some factor which would favor the onset of tachycardia, such as stooping, gastric flatulency, or sudden shock, was credited with initiating the painful seizure. Frequently the attacks occurred without apparent cause. The pain usually ceased with the disappearance of rapid heart action although at times aching in the substernal area persisted for a short time. The most common method of obtaining relief was the administration of morphine hypodermically, and then relief depended chiefly on the fact that vomiting ended the paroxysm. In the interval between attacks of rapid heart action only two patients complained of moderate stabbing pains in the precordium related to exertion. Five patients were moderately dyspneic during the intervals between attacks.

Some of the attacks of paroxysmal tachycardia and pain were ushered in by temporary vertigo and blindness, and in two cases by loss of consciousness. In a previous report[2] the occurrence of cerebral symp-

toms in paroxysmal tachycardia was discussed. The association of cerebral symptoms with attacks of pain similar to those in angina pectoris should always lead to an attempt to elicit a history of paroxysmal tachycardia as a possible cause of the pain.

The prognosis in cases in which there is pain during attacks of paroxysmal tachycardia is determined by the type and degree of the underlying cardiac lesion as determined by the ordinary methods of examination. The prognosis is apparently much better than that in cases of angina pectoris, inasmuch as the average duration of time that the patients in this group had suffered with pain during paroxysms was eight and a half years.

Six cases in this group were traced. Two patients were well, and two were in fair health although they still suffered from paroxysmal tachycardia associated with pain. Two patients died. One had chronic endocarditis with mitral stenosis and insufficiency and continued to have frequent prolonged attacks of paroxysmal tachycardia until death six months after examination. The other was a man, aged fifty-two years, who had suffered from marked cardiac dilatation with hypostatic congestion and pneumonia (during an attack of nodal tachycardia) while under our observation. These severe attacks continued, with development of edema of the lungs. The patient's home physician attributed death to multiple pulmonary infarcts.

The following abstracts of the records of seven patients illustrate the essential characteristics of the clinical picture.

CASE 1.—A woman, aged fifty-three years, had for twelve years been subject to attacks of rapid heart action lasting from ten to thirty minutes, terminating in momentary blindness and followed by great weakness. After the death of her son four years previously, she began to have pain with the seizures of tachycardia. The attacks lasted as long as twelve hours and were sudden in onset and cessation. They were accompanied by almost unbearable precordial pain which radiated into the left arm between the elbow and wrist, and also by a sense of impending death. While in the hospital under observation she had several similar attacks, and an electrocardiogram taken during a seizure showed nodal tachycardia, the rate being 196. The systolic blood pressure taken during an attack was 100 mm., and the diastolic 65 mm. Nitroglycerin did not relieve the patient, but morphine sulphate administered hypodermically in ¼-grain doses relieved her in ten minutes.

The patient weighed 133 pounds, and she gave her normal weight as 155 pounds. The systolic blood pressure was 165 mm., and the diastolic 78. The pulse rate varied from 78 to 96 a minute. The urine was normal. The hemoglobin by the Dare method was 30 per cent. The erythrocytes numbered 2,920,000 and the leucocytes 4,300 for each cubic millimeter of blood. The differential count did not show anything abnormal. The blood Wassermann test was negative. The fundus oculi showed evidence of moderate arteriosclerosis and anemia. There were marked pyorrhea and moderate periapical dental infection. Roentgenograms of the chest, colon, and stomach were negative. A fractional analysis of a test-meal revealed achlorhydria. There was considerable splenic enlargement. The basal metabolic rate (two readings) was +23. The patient left the hospital before the physicians had observed her long enough to decide on the cause of the anemia or the splenomegaly. Hyperthyroidism

was carefully considered, but the grounds for a clinical diagnosis did not seem sufficient. A diagnosis was made of paroxysmal tachycardia with severe cardiac pain. The patient was heard from one year and four months later, at which time she considered herself practically well. She wrote that she had gained 25 pounds, no longer had pain in the chest, and was subject to only slight attacks of rapid heart action. She attributed her cure to the use of mineral water.

CASE 2.—A woman, aged fifty-two years, had been subject to attacks of pain in the precordium with radiation into the left arm. For the first year the attacks came on at intervals of from two to three months, but during the last year they had been occurring every two to four weeks. At first the pain subsided after about one hour of rest, but later four or five hours of rest were required. The patient recalled that an attack always began with a sudden onset of rapid heart action and ended with a gradual return of the heart action to normal. Between attacks hurry and hard work did not bring on pain.

The patient's height was 5 feet, 7.5 inches, and the weight 196.5 pounds. The systolic blood pressure was 170 mm., and the diastolic 110 mm. The pulse rate was 84. The left ventricle of the heart was slightly hypertrophied. There was a marked systolic aortic murmur, and the second aortic sound was accentuated and tympanitic. The urine contained a trace of albumin, and a few pus cells in each field. The blood was normal, and the blood Wassermann test was negative. The fundus oculi showed moderate sclerosis of the retinal vessels. The blood urea was 28 mg. for each 100 c.c. The intravenous phenolsulphonephthalein test gave a return of 45 per cent in two hours. Roentgenograms of the chest showed slight hypertrophy of the left ventricle. The electrocardiogram revealed a rate of 90, slurring of the QRS complex in Derivation II, inversion of the T-wave in Derivation III, and left ventricular preponderance.

CASE 3.—A woman, aged forty-nine years, had been subject to attacks of rapid heart action for twenty-seven years. The attacks began suddenly and usually ended suddenly, lasting from a few minutes to thirty-six hours. During the last fifteen years pain had developed during the attacks. When the attacks ended abruptly pain appeared in the left side of the neck and down the left arm. The pain experienced during an attack was in the upper sternal region and radiated into both shoulders and down the left arm; the pain was most severe in the deltoid region and at the left elbow. Nitroglycerin and amyl nitrate did not afford relief, a hypodermic injection of codein usually being required. The patient was not observed during the attacks, but her home physician said that the pulse rate during the attacks was about 200.

At examination the pulse rate was 80, the systolic blood pressure 154 mm., and the diastolic pressure 94 mm. The urine and the blood were normal. There was evidence of marked periapical dental infection. The fundi revealed moderate retinal arteriosclerosis. Evidence of a cardiac lesion was not found. An electrocardiogram disclosed inverted P- and T-waves in Derivation III, sinus rhythm and left ventricular preponderance.

CASE 4.—A man, aged thirty years, had had attacks of rapid heart action for nine years. At first the attacks occurred only four or five times a year, but later they had occurred about once a week, and during which the entire right side of the body felt "dead." There was pain in the left shoulder, left side of the head and eye, with a dull severe aching pain in the precordium and epigastrium. Morphine, which induced vomiting, afforded relief. The pain ceased about forty minutes after morphine was given, but it was often much longer before the heart action slowed. Breathing was labored during an attack.

The patient weighed 118 pounds; the normal weight was 127 pounds. The systolic blood pressure was 115 mm., and the diastolic pressure 60 mm. The pulse rate was

100. Cardiac lesions were not found. The urine and the blood were normal. The blood Wassermann test was negative. The fundi did not reveal changes in the retinal vessels. The tonsils had been removed and there was no evidence of dental infection. The heart appeared normal in the roentgenogram. The electrocardiogram revealed a rate of 100, an inverted T-wave in Derivation III, and left ventricular preponderance.

CASE 5.—A woman, aged seventy-two years, complained of attacks of rapid heart action, sudden in onset and cessation, of twenty years' duration. At first the attacks lasted thirty minutes; recently she had had one lasting three days. In the earlier attacks she lost consciousness; in later attacks she felt blind and dizzy. Severe precordial pain, for which narcotics were required, accompanied the attacks. The systolic blood pressure was 165 mm., and the diastolic pressure 95 mm. The pulse rate was 80. The urine and blood were normal; the blood Wassermann test was negative. The combined phenolsulphonephthalein test gave a return of 50 per cent in two hours. The roentgenogram of the heart showed slight widening of the left border and moderate aortic dilatation. The electrocardiographic tracing showed ventricular premature contraction, slurred QRS complex in Derivation II, notched P in Derivation I, inverted P and inverted T in Derivation III, and left ventricular preponderance.

CASE 6.—A woman, aged fifty-six years, complained of attacks of precordial pain with radiation into the left shoulder and down the left arm. She had come for examination twelve years previously complaining of precordial pain when she lay on the left side. The systolic blood pressure was 200 mm., and the diastolic pressure 120 mm. On admission two years later she stated that she had been having precordial pain with radiation into the left arm but not related to exertion. The systolic blood pressure was 190 mm., and the diastolic pressure 115. At the third admission three years later the patient's complaint was unchanged and the blood pressure readings were essentially the same. On the present admission, the fourth, there was an opportunity to observe her in an attack. She complained of faintness, with pain in the precordium, felt most severely in the left shoulder and in the left arm. She was covered with a cold perspiration and appeared to be in shock. The pulse rate at the wrist was not perceptible and the rate at the apex was 200 a minute. The systolic blood pressure was 95 mm., and the diastolic 85 mm. The next morning the patient was in good condition, the pulse rate was 80, the systolic blood pressure was 160 mm., and the diastolic pressure 116 mm. On close questioning the patient was able to recall that racing heart action had always been a precursor and accompaniment of the seizures of precordial pain except during the first two years when she had noted attacks of paroxysmal tachycardia.

The patient was obese, weighing 193 pounds, and was 5 feet, 3 inches tall. The urine contained a moderate amount of albumin and a trace of sugar on one occasion. The blood sugar was 160 mg. for each 100 c.c. The blood Wassermann test was negative. The roentgenogram of the chest did not reveal abnormalities and the shadow of the heart was of normal contour and size. An electrocardiographic tracing was not obtained during an attack, but one taken before the seizure showed a rate of 100, slurring of the QRS complex and inverted T-wave in Derivation III, and left ventricular preponderance. A diagnosis was made of paroxysmal tachycardia with pain simulating that in angina pectoris, essential hypertension, and obesity.

The patient was given 3 grains of quinidine sulphate three times daily. Five months later she said she had experienced only slight attacks of tachycardia and almost none of the former symptoms of pain.

DISCUSSION

In a previous paper[6] in which the cause of pain in paroxysmal tachycardia was discussed, it was shown that the group in which it appeared presented evidence of coexisting arteriosclerotic processes affecting the

blood supply of the heart. In the cases in the present study, pain occurred in several instances in which it did not seem likely that such arteriosclerotic processes interfered with the blood supply of the heart.

Barcroft, Bock, and Roughton,[1] in a study of the circulation of a patient in attacks of paroxysmal tachycardia, observed lowering of the minute volume to nearly one-third its normal value. The systolic output of the heart was decreased from 77.5 c.c. to 12.9 c.c. during the attack. There was no reduction in the degree of saturation of the arterial blood, but there was a high degree of saturation of the mixed venous blood, the latter observation depending, in their opinion, on slowed circulation. Carter and Stewart[3] studied the blood gases in a case of auricular paroxysmal tachycardia and noted marked decrease of the degree of arterial saturation, low oxygen saturation of the venous blood, and greatly increased coefficient of utilization during the paroxysm, indicating a slow rate of circulation. Stewart and Crawford induced regular tachycardia in dogs and found that the blood flow was usually unchanged, but that in one-third of the observations it was decreased, and about the same proportion of animals showed a decrease of from 4 to 7 per cent in the oxygen saturation of the arterial blood. Smith, Miller, and Graber[4] have shown in dogs, "that the maintenance of an efficient coronary circulation is fundamentally dependent on the height of the diastolic pressure" and that the changes in the systolic pressure play a subordinate part in its influence on coronary circulation.

If it may be assumed that coronary circulation, insufficient either in amount or in oxygen saturation, is a predominant cause in the production of cardiac pain, then the described investigations furnish, in spite of certain divergent conclusions, sufficient basis for believing that impoverishment of the coronary circulation and myocardial fatigue are the cause of the pain observed in these cases.

In the two cases in this series in which the blood pressure was taken during seizures, there was a marked drop in the systolic and a definite drop in the diastolic. This is in accord with four other cases not included in this series, in which the blood pressure was obtained during paroxysms. Correlating this observation with the investigations of Smith and his coworkers, it is logical to assume that there were marked changes in the coronary blood flow. Moreover, any pathological process impairing the normal capacity and function of the coronary arteries, such as arteriosclerosis, would render the threshold of pain production lower in proportion to its effect on the coronary circulation. The fact that most patients escape cardiac pain in attacks may have a partial explanation in the observations of Stewart and Crawford,[5] and probably indicates that blood flow and oxygen saturation of the arterial blood in these patients may be changed little or not at all during the paroxysms.

SUMMARY

Nineteen cases of paroxysmal tachycardia were studied in which the pain was similar in type and location to that seen in cases of angina pectoris. The pain is chiefly distinguished from that of angina pectoris by the absence of the relation of the pain to factors which precipitate attacks of angina pectoris, and also by the fact that the painful seizures tend to occur over a long period of years without a serious outcome. The diagnosis rests on the demonstration of evidence that the pain is an accompaniment of attacks of paroxysmal tachycardia. In contrast to the pain of angina pectoris, except that which occurs in coronary occlusion the pain in paroxysmal tachycardia has a much longer duration as a rule.

The prognosis depends on the type and degree of underlying cardiac injury, but in general is good if there is no other cardiac disorder.

Treatment of the pain which occurs with attacks of paroxysmal tachycardia consists in measures which have as their objective the control of the paroxysms of rapid heart action.

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PAROXYSMAL CARDIAC PAIN*

The Syndrome in Young Adults with Rheumatic Valvular Heart Disease

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SEVERE paroxysmal pain of the characteristic cardiac type is not very common in young adults with chronic rheumatic cardiac valvular disease.[1] The few observations mentioned in the literature[2, 3, 4] have received but passing notice. This has been partly due to the varied symptoms and signs presented by these patients when seen as isolated instances.

Within the past few years, there have been admitted to the wards of the Montefiore Hospital five young adults with an antecedent history of rheumatic fever whose main presenting complaints were severe recurrent attacks of paroxysmal cardiac pain. While the symptom complex has been variable in each particular case, the clinical picture of all, as observed over a prolonged period of hospitalization, has been so strikingly uniform that it has been thought worth while to describe these cases in detail. The prognosis as to life of these younger patients with paroxysmal pain associated with chronic valvular lesions appears to be better than that of older patients with so-called angina pectoris.

Case 1.—History No. 10296 R. Diagnosis: CRCVD†, aortic insufficiency, mitral stenosis and insufficiency, cardiac hypertrophy.

M. S., a girl aged sixteen years, was admitted to the hospital on August 21, 1922. Her chief complaints were recurrent attacks of severe substernal pains and shortness of breath.

Previous History.—At the age of four she had an attack of acute articular rheumatism which forced her to remain in bed for several months. At the age of twelve, she had tonsillitis, followed by a tonsillectomy several weeks later. In the few months prior to admission she experienced repeated attacks of severe substernal pains accompanied by fainting spells during or after the seizures. These came on without any warning and awakened her out of sleep during the night. At other times they occurred when she was up and about carrying on her daily routine. The attacks would last from a few minutes to one hour and always subsided as suddenly as they appeared, leaving her in an exhausted condition. During the attacks, she felt a fullness in the head, violent palpitations of the heart, marked throbbing of the vessels of the neck, and severe pains in the substernal and precordial regions, radiating to the arms and back, but never to the ulnar side of either arm. All of these symptoms would come on together so that she could not tell which appeared first. There was at no time any sensation of impending dissolution. She never vomited with these attacks and, as far as she could remember, she had never noticed any swelling of her feet after them. In the intervals between recurrences she exprienced occasional fainting spells.

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†CRCVD stands for chronic rheumatic cardiac valvular disease.

Physical Examination.—On admission the patient appeared to be a fairly developed and nourished girl. Her face was flushed, and there was moderate cyanosis of the lips. The heart was enlarged in all directions and showed signs of mitral stenosis, and insufficiency of the mitral and aortic valves. The pulses were equal and regular and collapsing in type. The blood pressure was 190/120. The lungs were negative. The abdomen was soft. The liver and spleen were not palpable. The legs showed no edema.

The laboratory findings including the blood Wassermann reaction were negative.

The radiographic examination of the chest failed to show any abnormality of the lungs. The heart showed enlargement both to the right and to the left, most marked in the region of the left ventricle. Cardiac dimensions were M. R. 6.2 cm.; M. L. 10.4 cm. The electrocardiogram showed left ventricular predominance. The T-wave was negative in Leads I and II. (Patient was not receiving any digitalis.)

Course and Description of the Attacks.—During the first two months of her stay in the hospital the patient was up and about most of the time. On October 7, 1922, she had her first attack of severe substernal pain, such as she had experienced at home. She had been out of bed most of the day, only occasionally complaining of sharp, lancinating pains passing down both her arms. She felt that on that particular evening she would have an attack. For this reason a member of the staff remained in the wards to watch her through one of the seizures. At about 10:40 P.M., while asleep, she was suddenly awakened by a sharp retrosternal pain which radiated down both arms. The pains were vise-like in nature, constricting her chest in the form of a girdle. Palpitation of the heart was marked and there were violent pulsations of the vessels of the neck. There was no belching, and she did not vomit. There was slight sweating but no other associated vasomotor phenomena. The blood pressure readings taken soon after the attack started were as follows:

TIME	B. P.	REMARKS
10:42 P.M.	210/160	The pain was severe at this time
10:43	215/155	
10:44	215/150	Ampule of amyl nitrite given
10:44+	120/70	There was some relief of pain
10:44/30	165/50	
10:45	190/80	
10:45/30	240/90	
10:46	250/80	
10:47	238/90	Pain as severe as before
10:49	230/80	" " " " "
10:52	235/150	" " " " "
9:40 A.M. next morning	195/145	Up and about the wards as if nothing had happened

After twenty-five minutes the pains disappeared as spontaneously as they were ushered in, without any other medications. Throughout the seizures, the pulse rate was elevated to over 160 beats per minute, and the respirations were very rapid. The heart sounds were very loud, and the aortic second sound was accentuated. The lungs, however, were perfectly clear. The liver edge was not palpable.

Between the first attack and her discharge from the ward, she had about six similar attacks varying in severity and duration. During one of the milder seizures, she complained of a choking sensation and a heavy feeling substernally, as well as the characteristic pains described above. Examination of her chest during this attack revealed both large and fine moist râles over both bases posteriorly.

Since her discharge from the hospital, the patient has been at work as a stenographer almost all the time. There have been no recurrences of attacks except on one occasion when after some moderate exertion through the day she had a fainting spell in the evening with a choking sensation accompanying it. The administration of amyl nitrite cleared up her symptoms and she was well enough to be able to dance

on the following day without any distress. She is still under observation, although at present she presents no symptoms. Her blood pressure is 190/130.

It is interesting to note in this case the persistent high diastolic pressure over a long period of time without any accompanying signs or symptoms of renal insufficiency.

At no time during her stay in the hospital was there any rise in the temperature curve, and she has never up to the present day shown any signs of decompensation.

CASE 2.—History No. 8227. Diagnosis: CRCVD, aortic insufficiency, mitral stenosis and insufficiency.

A. S., a young adult male, aged twenty years, was admitted to the hospital on September 26, 1921, complaining of severe precordial pains, shortness of breath and palpitation of the heart.

Previous History.—He was perfectly well up to two years prior to admission, when he had his first attack of acute articular rheumatism with high fever, swelling of the joints, and prostration (October 6, 1919). Because of the severity of the symptoms, he was removed to a hospital where he remained for the following nine weeks. In May, 1921, about one and one-half years after his first illness, he had a recurrence and was again compelled to stay at a hospital for about ten weeks. After a short convalescence in the country following his second discharge, the patient was admitted to our institution.

Physical Examination.—On examination, he proved to be an undernourished and poorly developed young man, weighing only 104 pounds. He was of the asthenic habitus, with long, narrow chest and cold, moist, cyanotic hands. His face was flushed but showed a well-defined circum-oral pallor. The eyes were prominent. The Von Graefe sign was negative. The vessels of the neck were pulsating, and there was a diffuse heaving impulse of the precordium and nodding of the head with each heartbeat. His heart showed definite enlargement, with involvement of both the mitral and aortic valves. The pulses were equal and regular and collapsing in type. The rate was 90. The Duroziez sign was positive, and the capillary pulsations were very marked. The lungs were clear. The liver and spleen were not palpable. The legs showed no edema.

Radiographic examination of the chest showed the lungs to be clear. The heart was enlarged in all directions. Cardiac measurements were M. R. 4.2 cm.; M. L. 11 cm.

The electrocardiogram showed left ventricular predominance. There was negativity of the T-wave in both Leads I and II. (Patient had not been receiving digitalis.)

Course and Description of a Typical Attack.—One evening, about a month after admission (November, 1921) the patient was suddenly awakened by a sharp substernal pain in the region of the third and fourth ribs. At first he felt a pressing from within outwards, but as the pain became severe it radiated to the back of the shoulders and was felt more on the right side than on the left. Later, during the attack, there was radiation to both arms and to the right elbow posteriorly. The pupils were widely dilated, the cheeks were flushed. There was dilatation of the alae nasi, and the respirations were labored. The carotids were pulsating violently. The forehead was covered with large beads of cold perspiration, and the face assumed a haggard and worn expression, with the cheeks sunken in. The patient could not sit still because of the cramp-like nature of the pain which became worse as the attack

TIME	PULSE	RESP.	B. P.	PAIN
8:28 P.M.	108	32	220/0	Substernal and back of shoulders
8:35	92	30	229/0	Amyl nitrite inhaled
8:40	100	30	130/0	Pain gone
8:42	100	15	210/0	Pain reappearing in right elbow
8:46	100	22	220/0	
8:57	90	28	220/0	Pain persisting in right elbow
9:07	90	26	210/0	

continued. He asked to be allowed to be up and about the ward, for he felt that walking would relieve him.

The pulse, respiration, and blood pressure at this time are given on p. 499.

This attack lasted about one hour and a half before it receded.

A similar study of the blood pressure was carried out during an attack that came on about one week later, with the following results:

TIME	PULSE	RESP.	B. P.	REMARKS
10:45 P.M.	120	28	210/0	Exact spot of pain was 4 cm. above the xiphoid in mid-sternal region
10:55	120	28	125/0	Amyl nitrite inhaled. Pain left momentarily
11:05	105	28	205/0	Pain returned with increasing severity. Nitroglycerin gr. 1/100 placed under tongue
11:19	94	24	155/0	
11:25	90	24	145/0	
11:35			140/0	
11:45			135/0	Pain gone completely

Repeated attempts to effect the same lowering of blood pressure during other attacks by means of nitroglycerin produced absolutely no changes. Throughout the entire attack there were moist râles all over both bases posteriorly as far up as the axilla on both sides. On the following morning the blood pressure was 135/0, and his lungs were clear. There was no enlargement of the liver, and the legs showed no edema.

Progress.—During his stay at the hospital the patient had several severe and other lighter seizures of a nature similar to those described above. Each time the pain and blood pressure changes came on together, so that it was impossible to state which was first. The highest systolic blood pressure recorded in him was over 300 mm. of mercury at the height of a very severe attack which lasted over three hours. In the interval between the attacks, he would feel perfectly well and carry on normal activities as if there were nothing wrong with him. Attention is also called here to the fact that at no time throughout his period of observation was there any rise in his temperature.

Five years after the onset of his first symptoms, the boy is working in an office. He is free from any seizures similar to those he had while under observation. At no time since the onset of his illness have there been any signs of cardiac failure except slight shortness of breath on climbing stairs.

CASE 3.—History No. 9791. Diagnosis: CRCVD, aortic insufficiency, mitral stenosis and insufficiency.

B. N., a young girl,[2] aged sixteen years, was admitted to the hospital on June 7, 1919. Her chief complaints were shortness of breath, and frequent, recurrent attacks of severe substernal pains.

Previous History.—The first signs of heart disease in her were noted at the age of eleven. In the four months prior to her admission here, the patient was having about two or three attacks of substernal pains daily. Sometimes these would wake her out of sleep, and after lasting from one-half to one hour they would end spontaneously but leave her in a weakened condition. Constant pains in the shoulder and back would remain for hours following such a major seizure. More often, gnawing pain in the back between the shoulder blades would be the only symptom for days. The severer attacks came on as she was retiring. Frequently they were worse when she was in the reclining position. Nausea and vomiting never accompanied these symptoms, but violent throbbing of the vessels of the neck and forcible palpitations of the heart were always prominent during a seizure. Headaches at these times were unbearable; they were mainly frontal in type. She never actually fainted although

she felt she might many times when the pains were severest. She noted her hands were blue and felt cold at the height of the attack.

Physical Examination.—The girl was poorly nourished but appeared comfortable as she was sitting in bed. There was slight dyspnea and moderate cyanosis of the lips. The vessels of the neck were throbbing violently, and the chest showed a heaving pulsation with each heartbeat. The heart was enlarged, and there was evidence of both mitral and aortic lesions. The pulses were equal, regular, and Corrigan in type. There was a pistol-shot femoral sound and marked capillary pulsations. The blood pressure was 140/0. The lungs were clear. The liver and spleen were not palpable. There was no edema of the extremities. The blood Wassermann reaction was negative.

Radiographic examination of the chest failed to reveal any abnormalities of the lungs. The heart showed a moderate enlargement, most marked to the left. Cardiac measurements were M. R. 4.7 cm.; M. L. 11.4 cm.

The electrocardiogram showed left ventricular predominance. T^1 and T^2 were negative.

Course and Progress.—In the first five months of her admission to the wards, the patient was comfortable and attended to her studies in the hospital school. At the expiration of this time she began to have a series of attacks of substernal pains which kept her in bed for the following year. She became extremely irritable. The slightest emotional disturbances upset her very quickly so that she experienced violent palpitations of the heart with severe precordial oppression. A dilatation of the right subclavian artery each time she had these attacks caused her considerable worry. When seen during one of these seizures, the patient was extremely cyanotic. The face, lips, ears, and fingers were almost black. Dyspnea was marked. The respirations were labored. The pulse rate was rapid and thready. There was violent pulsation of all the peripheral vessels. She complained of headaches and pains which started with the attacks in the region of the second and third left costosternal junctions and passed backwards to the shoulder blades and down the left arm as far as the elbow but not to the fingers. She never complained of radiation to the right. Preceding, during, and subsequent to the attack, her left chest presented anteriorly and posteriorly an area of hyperesthesia between the first rib and the level of the xiphoid. On one occasion marked epistaxis relieved her headache and ended very abruptly the attack of pain. Seventeen separate attacks were somewhat relieved each time by venesection. At no time during these periods was there any rise in temperature, and no signs of cardiac insufficiency were ever noticed except her intense cyanosis. In three years' time her liver edge descended only two fingerbreadths below the costal margin, to recede eventually when she became free from symptoms. The blood pressure throughout the attack was always over 300 mm. and was never influenced by phlebotomies. Her symptoms, however, were considerably ameliorated by this procedure.

Frequently the onset of the attack of pains was preceded by a feeling of numbness over the entire left upper extremity and tingling and numbness over the left lower limb. For a period of over six months she complained of frequent menstruation coming on profusely every ten days and lasting six days at a time.

During the presence of these symptoms she had a very severe attack at one time

TIME	B. P.	PULSE	RESP.
7:40 P.M.	220/0	114	30
8:00	210/0	96	30
8:07	212/0	84	30
8:10			
8:13	285/0	128	
8:15	295/0	132	
8:23	240/0	160	30

(12/4/21) which started with intense shooting pains down the right arm. She assumed a position with the head in extreme opisthotonus. The face was a deep bluish red, and her body and extremities were seen to pulsate with each ventricular systole. The heart sounds were loud, but the murmurs were practically inaudible because of the rapid rate.

There were a few moist râles over both bases posteriorly and throughout this seizure the patient changed position continually, which accounts for the variations in blood pressure obtained (see discussion). The pains disappeared spontaneously an hour after their onset. On the next morning she was attending classes in the hospital school.

Eight years after the onset of the first attack, the patient is working as a clerk and free from symptoms except the slight dyspnea which she experiences on exertion. She has been free from pain now for four years, although several attacks of cyanosis have been relieved by venesection of one pint.

CASE 4.—History No. 13647. Diagnosis: CRCVD, aortic insufficiency, mitral stenosis and insufficiency, cardiac hypertrophy.

D. G., a boy aged sixteen years, was admitted to the hospital on April 8, 1926. He complained chiefly of constant pains in the shoulders and arms, recurrent attacks of severe substernal pains, palpitation of the heart, and shortness of breath.

Previous History.—The patient was well up to 1918 when he had a severe attack of influenza during the epidemic of that year. In 1921, he had his first symptoms of acute articular rheumatism which confined him to bed for six weeks. Following convalescence he was able to be up and about for the ensuing two years without complaining of any illness. In the summer of 1924 he contracted bronchopneumonia, complicated by pleurisy with effusion, which cleared up after several months of convalescence. Since his last illness he has never been well enough to carry on normal activities.

Physical Examination.—On admission, the boy appeared very pale and undernourished but comfortable enough to sit up in bed. He was tall, narrow-chested, with moist and clammy hands. His face was pale, but his cheeks were highly flushed. The veins of the neck were slightly distended. His heart was tremendously enlarged to the left, the apex being in the seventh intercostal space. The pulses were equal and regular. The Duroziez sign was positive, and the capillary pulsations were prominent. Almost all of the peripheral vessels were throbbing. The blood pressure was 130/0. The lungs were clear. The liver edge was 3 cm. below in the midline. The spleen was not palpable. There was no edema of the extremities. The blood Wassermann reaction was negative.

Roentgen examination of the chest failed to show any abnormality of the lungs. The heart was markedly enlarged, especially in the region of the right auricle. Cardiac measurements were M. R. 6.2 cm.; M. L. 14.2 cm.

The electrocardiogram showed right ventricular predominance, a prolonged P-R interval to 0.24 sec., and some evidence of intraventricular conduction disturbance. The P-wave was widened and notched in the first two leads.

Course and Progress.—On the fifth day after his admission to the hospital he began to complain of generalized abdominal cramps and umbilical tenderness. His temperature at this time was 98.6° and his pulse rate 96. A subicteric tint to his skin appeared. His pains disappeared on the administration of mild sedatives only to reappear with increasing severity about one week later.

The following is a description of a typical attack. The boy was lying in bed with his head resting on a pillow and his hands on his abdomen. He complained of severe generalized cramp-like abdominal pains. He was nauseated and tried to vomit but was unable to do so. His face was of a ghastly color, almost white. He was perspiring profusely. The vessels of the neck were pulsating violently. There was

marked enlargement of the superficial veins of the neck which became enormously distended on pressure over his liver area. These remained filled for about five minutes after the release of pressure. The entire chest was heaving with each heartbeat. On questioning he stated that the pains came on suddenly and started at first in the small of the back and gradually travelled forward to the region of the umbilicus where they seemed to remain in the form of a "lump." They were constant, and with their onset he experienced forcible palpitation of the heart and throbbing in his head. He had never felt so badly before. At first he had to double up, but finally he found that by extending his head far backward he could be greatly relieved. The temperature was normal. His blood count showed no increase in the neutrophile cells, and his urine remained unchanged. His blood pressure taken at this time was 300 mm. systolic. The diastolic could not be obtained. The administration of amyl nitrite made him feel worse and nitroglycerin produced no relief. Morphine quieted him a bit but did not influence the blood pressure. The pain receded, to recur again in spasms and after an hour of excruciating suffering it finally passed away. With the cessation of his symptoms the blood pressure fell to its normal figures of 140/0, three hours and twenty-two minutes after the onset of the major attack.

During this attack, many râles were heard over his chest. On the following day percussion of his heart revealed no increase in size and a teleroentgenogram, compared with that taken on admission, showed no change.

Pin-prick examination of his chest after the attack showed a well demarcated area of hyperesthesia between the second and last ribs on the left side anteriorly and between the second and twelfth dorsal segments on the same side posteriorly. The skin over the abdomen was not hypersensitive.

Electrocardiograms taken before, during, and after the attack failed to reveal any changes in the complexes from the original records. The rate, however, was increased to 120.

Two days after this severe seizure, he began to show edema of the extremities and the back. With the onset of these signs, his abdominal pains passed away for the time being, although nausea and vomiting persisted. The abdomen, however, was soft, lax, and the liver edge was now 6 cm. below the costal margin in the midclavicular line. On the following day, he complained of pains in the arms and shoulders. These were constant, localized and persistent, and were only relieved by morphine.

Despite the onset of dropsy, he had a few more severe attacks of a similar nature to those described, and finally died from cardiac failure one month after admission to the hospital ward. In the last attacks, however, the pains had their onset substernally, with radiation to both shoulders and right elbow posteriorly. They lasted as long as two hours each, were accompanied by severe rises in the blood pressure (300 mm. systolic), and were relieved only after the administration of large doses of opiates. (No autopsy.)

CASE 5.—History No. 13363. Diagnosis: CRCVD, aortic and mitral insufficiency.

L. Z., a boy, aged nineteen years, was admitted to the hospital on January 8, 1926. His chief complaints were recurrent attacks of "burning" and "sticking" substernal pains, weakness, and dizziness. At times during these seizures he had very severe headaches.

Previous History.—Five years prior to admission, the patient had his first symptoms of acute articular rheumatism. He was admitted at that time to the Long Island College Hospital where he remained for four weeks. For two years following his first illness he was perfectly well except for occasional sticking pains in his joints. Then he had a severe recurrence of his articular rheumatism which also involved the joints of his hands. He was readmitted to the hospital and remained there for twenty

weeks. On discharge his heart was well compensated and remained so for a period of one year, when he started to complain of attacks of precordial pains that radiated to the left arm. These were sticking and gripping in nature. They came on at all times without any warning and were worse when he was in bed. No medication seemed to help him. In the intervals between these seizures he was well and out of bed all the time. One month before he was transferred to our medical division, and when all other measures had failed to relieve him, paravertebral block with novocaine and alcohol of the third, fourth and fifth left dorsal roots and their rami communicanti, was performed.

Physical Examination.—The patient was a very pale, tall, poorly nourished, narrow-chested young man who appeared in great distress. He had a marked acne of the face. His hands were moist and cold. He was propped up on pillows but there was no dyspnea. Cyanosis of his lips, eyelids, and finger nail beds were very marked. There were a few large exanthematous spots on his chest, but no petechial spots were visible anywhere. The vessels of the neck were pulsating tumultuously. There was slight distention of the superficial neck veins. His heart was enlarged and showed evidence of both mitral and aortic disease. The pulses were equal and regular and collapsing in type. The blood pressure was 160/0. The lungs were clear. The abdomen was soft and lax. There was palpable pulsation of the abdominal vessels. Liver and spleen were not felt. There was no edema of the extremities.

The roentgen examination of the chest showed a slight increase in the lung markings due to congestion. The heart was markedly enlarged especially in the region of the left ventricle. Cardiac measurements were M. R. 5.4 cm.; M. L. 13.1 cm. The electrocardiogram showed left ventricular predominance. There was negativity of the T-wave in both Leads I and II. (The patient was not receiving any digitalis.)

Course and Progress.—The patient remained with us only one month. During that time we had occasion to observe him through several attacks of severe precordial pain. Throughout his stay in the hospital these would come on only at night, usually at about 11 P.M. Assuming a crouching position, he would scream out with pain which in his case was sudden in onset and started about the middle of the sternum, passing to the back and shoulder blades, but never radiating to the arms. He felt considerable relief from belching or moving about. With the onset of pain there were violent pulsations of the peripheral vessels. He began to sweat profusely; his face and neck would redden and a diffuse erythematous patch would appear over his chest. This persisted after the disappearance of his pains. The blood pressure mounted to over 300 mm. at the height of the attack. Its subsidence would take place slowly and spontaneously without the aid of any medication. Despite extensive bilateral paravertebral block there was a definite area of hyperesthesia over the entire anterior aspect of the chest from the second to the sixth ribs, and posteriorly he was sensitive to pin prick in the region of the left third, fourth, fifth, sixth and seventh intercostal areas. His lungs remained comparatively clear throughout these observations. The temperature was slightly elevated during one of his seizures, but the leucocytes at this time were never increased.

TABLE I

CASE NO.	AGE	SEX	AGE AT ONSET OF RHEUMATIC FEVER	TIME SINCE LAST ATTACK OF RHEUMATIC FEVER	AGE AT ONSET OF PAROXYSMAL PAIN	DURATION OF CRITICAL PERIOD	TIME SINCE FREED FROM PAIN
10296	16	F	4 years	4 years	16 years	1 year	5 years
8227	20	M	18 years	6 months	20 years	9 months	6 years
9791	16	F	?	?	15½ years	1 year	8 years
13647	16	M	11 years	3 years	16 years	1 month	Died*
13363	19	M	14 years	2 years	16½ years	9 months	1 year

*Died presumably from myocardial degeneration.

The patient left the hospital, and when last heard from was at home still having the attacks but not as frequently as when under hospital observation.

DISCUSSION

From a description of these cases it is obvious that the various manifestations which they exhibit place them in a different category from that of patients with classical symptoms of so-called angina pectoris. (See Table I.)

Their age incidence is of extreme importance. All of them were between fifteen and twenty years old when the major syndrome made its first appearance. They have all been subject to recurrences and exacerbations of acute articular rheumatism. Nevertheless, despite their advanced organic heart lesions, these patients have usually remained free from fever during this crucial period and have appeared less subject to rheumatic reinfections subsequently than other young patients with similar rheumatic valvular lesions.

The majority of them are the long, narrow-chested poorly developed type. They usually complain of cold feet and hands and increased perspiration. They are extremely irritable during the time of the attacks, highly emotional, and disturbed by their surroundings. Sometimes they are the opposite in disposition, i.e., sulky and melancholic. Often they show spontaneous vasomotor disturbances in the form of erythematous patches that appear on their necks and chests, to persist there till the attack of pain is over. Even when these "crises" have ceased and run their course, they still exhibit periods of profuse diaphoresis.

THE MAJOR SYNDROME

The attacks for which they seek relief are characterized by recurrent seizures of paroxysmal chest pains; violent palpitations of the heart; severe headaches and varied associated vasomotor phenomena; marked pulsations of the peripheral vessels; paroxysmal rises in blood pressure, and increase in pulse rate and respirations.

The attacks may make their appearance anywhere from one-half to twelve years after the first manifestations of rheumatic fever. The heart invariably presents multiple involvement of the valves and all cases show marked incompetence of the aortic valve. Signs of decompensation are usually absent. The seizures vary in number anywhere from six to sixty in a single year and may last from one-half to three and a half hours at any one time, over periods as short as one month and as long as two years. They have never been noted during an active bout of temperature and they have seldom been preceded, accompanied or followed by any rise in temperature. Likewise, the neutrophile count has never been abnormal. Emotional disturbances enhance these attacks, but effort relieves them and bears no relationship to their onset. On the contrary the dreaded hours of the night and rest increase their severity. In girls, menstruation seems to influ-

ence them somewhat, and in one patient repeated epistaxes were a relief. Occasionally the patients are conscious that an attack is about to come on. Their only wish is to be relieved from the excruciating pain which is the chief presenting symptom.

THE PAINS

The pain is paroxysmal in type and is considered cardiac in origin because of the close relationship to the accompanying vascular phenomena, as well as the characteristic distribution of the areas of hyperesthesia following the attack. Its onset is usually sudden and without warning. It makes its appearance mainly at night or when the patient is about to retire. Rest fails to alleviate but effort seems to relieve the pain. In this way it differs radically from the severe paroxysms of cardiac pain induced by effort. It bears no relationship to meals. It is never preceded by nausea or vomiting and is never followed by any desire to urinate. In one case a severe dysuria, grave enough to demand catheterization, followed an attack.

The pain frequently starts in the mid-sternal region about 4 to 6 cm. above the xiphoid. It may commence in the abdomen a little above the umbilicus and simulate visceral colic. In one case it was mistaken by the surgeons for an acute abdominal condition. It has been described as "cramp-like," "vise-like," and as "if something from within was pushing the chest outward." Localized at first in its place of origin it may radiate in various directions to the back between the shoulder blades, or to the neck and arms as far as the elbows, but not to the ulnar side of the forearm and fingers. It may be localized near the region of the appendix or around the left kidney. The pain is never accompanied by any anguish or feeling of impending death.

No matter where the onset or radiation of the pains may be, the area of hyperesthesia delineated on the body following an attack is usually restricted to both the anterior and posterior left half of the chest and part of the inner aspects of the left arm. There are no distinct sore spots.

The pain during the attack fluctuates in its severity and may be slightly relieved by effort, posture, belching, and frequently by the administration of the nitrites. Some cases are made much worse by the drug if they are refractory to it. Others are not affected at all by its administration and the pain in those cases recedes spontaneously.

In what appears to have been a similar example in a boy sixteen years old (with signs of incompetence of the aorta and no evidence of decompensation), Wenckebach[4] was able to obtain relief during an attack by the intravenous administration of ½ gram of quinine. At the same time he noted a marked fall in the systolic and diastolic blood pressure of this patient.

Cutler has recently described a boy eighteen years old with an ante-

cedent history of rheumatic fever, in whom he produced arrest of pain from such attacks by a modified bilateral cervical sympathectomy. In one of our patients bilateral paravertebral alcohol injections produced no immediate relief, although at present the patient is free from pain.

Once the major attacks disappear, the pains never recur. What does happen on severe exertion is a feeling of uneasiness localized about the precordial region. In one patient a sense of choking was the only sign of excessive effort. In her, as well as in one other patient, the administration of amyl nitrite at such times caused all symptoms to disappear very rapidly. The duration of these sensations is as long as that of the major attacks in the development of which the pains and blood pressure crises appear to be intimately related.

THE BLOOD PRESSURE CHANGES

With the exception of the first case, in which the cause of the high diastolic pressure remains unexplained it will be noted that all patients exhibit the high systolic and characteristic diastolic pressure of cases with aortic insufficiency. During the attack, the systolic blood pressure mounts up to over 275 mm. of mercury in each case. In some it is far above the 300 mark, the height of the rise depending upon the severity of the attack.

Paroxysmal cyanosis with marked distention of the superficial veins of the neck may be the first presenting symptom, possibly due to an increased intrapulmonic pressure.

The rise in blood pressure is sudden and comes on concomitantly with the onset of pain. We have been unable to register a fall in blood pressure preceding the rise. Once the rise has taken place, the systolic blood pressure is sustained with only slight fluctuations until the end of the seizure. The diastolic pressure, where it is measurable, shows similar changes.

Phlebotomy in these cases may relieve the violent headaches and abate the cyanosis but does not cause a lowering of the pressure at the height of the attack. Both the pains and the blood pressure are influenced temporarily by the inhalations of amyl nitric and the administration of nitroglycerin in cases favorably affected. Under the action of these drugs, in the nonrefractory cases, there is a sudden transition of both the systolic and diastolic blood pressures to figures even below the original reading, but as soon as the effects of the drugs are over, the mercury climbs again to its maximum figures to stay there until it recedes spontaneously with the cessation of the attack. It has already been mentioned that the pain recedes with the fall of blood pressure. The variations of the diastolic pressures have been noted to be less than those of the systolic both during the seizures and under the influence of the drugs.

Atropine has very little effect in changing an already existing rise, and in one case where it was tried the change was so gradual after an

intravenous injection ($\frac{1}{160}$ gr.) that it is doubtful whether or not the drug was responsible for the result.

Invariably the return of the blood pressure to its previous level is a slow and gradual one. There is generally no sudden change or fluctuation before the final drop, such as has been observed in fatal cases of so-called angina decubitus. When such variations have been noted, they were associated with, and probably due to, postural changes. The persistence of the systolic hypertension during an attack, with only gradual recrudescences in cases of paroxysmal cardiac pain, has been considered as a good prognostic sign by Lutembacker.

The systolic blood pressure, in the interval between the attacks, shows only a slight diurnal periodicity. Neither at rest, after exercise, nor at the height of the attack have we been able to register any alternation of the pulse.

In the residual attacks of uneasiness which come on long after the major seizures have ceased, the blood-pressure changes are present but only in mild degrees. The response to the nitrites at these times (in nonrefractory cases) is the same as during the pain attacks.

ASSOCIATED PHENOMENA

During the attack, the heart rate and respirations are increased almost simultaneously with the onset of pain. The patient becomes conscious of violent palpitation and the peripheral blood vessels distend with each forcible systolic pulsation. Some of the arteries assume an almost aneurysmal dilatation which is exceedingly annoying.

Dyspnea is marked, but there is neither inspiratory nor expiratory wheezing present. The breathing is rapid, the rate about thirty per minute, but deep. The lungs remain clear until almost the end of the attack, when occasionally moist râles begin to make their appearance at both bases posteriorly. There is no frank pulmonary edema as has been observed in several of our cases with other forms of paroxysmal cardiac pain.

We have been unable to discern any increase in the size of the heart chambers by x-ray examination during or after the attack, and the electrocardiograms taken at repeated intervals reveal no significant changes from the original. The heart sounds are loud; the murmurs are accentuated, but the rhythm is regular, and there is no gallop. In one case, studied by roentgenograms, the cardiac measurements were practically the same before as after a seizure.

The liver does not enlarge and its edge is not palpable except when other causes operate to produce heart failure. In the single fatal case described, the liver descended very rapidly, so that in the course of a week the edge was near the umbilicus. The liver is not tender at any time even on deep pressure over the costal regions. (It is important to bear this in mind in the cases that exhibit pain phenomena referred to the abdomen.) The spleen is usually not palpable.

The extremities remain free from edema and no thrombotic changes have been observed in them although tingling sensations and numbness make themselves evident at the onset of the variations in the blood pressure.

PROGNOSIS

Four of these patients are living, one, five, six, and eight years respectively after the typical critical periods of recurrent attacks of substernal pains. In these intervals of apparent comfort, there have been no similar recurrences and there has been practically full economic restitution. While it is too soon to judge of the final outcome as to life, it is certain that the prognosis for recovery and freedom from pains in these cases is very good. This is in contradistinction to other forms of paroxysmal cardiac pain on an organic basis, in which it is still impossible to predict the prognosis either as regards duration of pain or expectancy of life.

CONCLUSIONS

1. Five cases are reported of young adults between the ages of sixteen and twenty, suffering from chronic rheumatic cardiac valvular disease, whose main presenting symptom was severe paroxysmal cardiac pain during a certain critical period.

2. All of these patients had an antecedent history of rheumatic fever and all showed multiple valvular involvement of the heart of some duration.

3. The paroxysmal attacks of pain were mainly nocturnal in type and were accompanied by increased pulse rate and respirations, marked rises in blood pressure, violent pulsations of the vessels of the neck, severe headache, and variable vasomotor phenomena.

4. The onset of these attacks was always during an afebrile period and came on from one to twelve years after the first signs of rheumatic fever.

5. The recurrences of cardiac pain were observed to occur during a period of from nine months to one year in four successive patients. In a fatal case they were noted one month prior to death.

6. Four of the five patients are living, several years after the "crucial period," free from all symptoms of pain.

7. Such periods of recurrent precordial pain in young patients with chronic rheumatic cardiac valvular disease do not in themselves indicate a poor prognosis as to life.

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TREATMENT OF HYPERTENSION*

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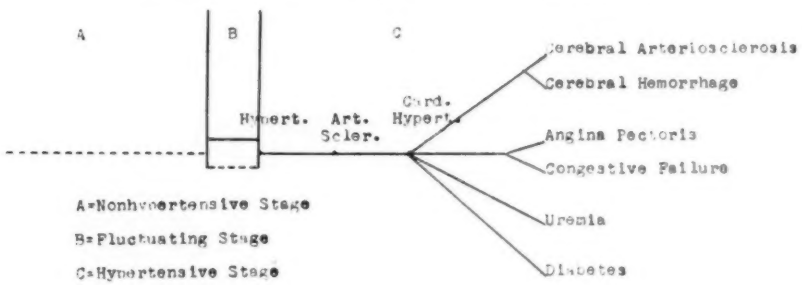
THE wording of my subject, The Treatment of Hypertension, is somewhat indefinite and I wish to state at the beginning that my remarks will be confined to the treatment of what is known as vascular hypertension. Of necessity, closely related subjects will be touched upon, but no attempt will be made to discuss the treatment of all phases of the hypertensive problem. As in all disease, the treatment starts with knowledge; in this case the knowledge of the origin and development of the vascular disorder and the interrelationship of its various parts. It may be assumed with a reasonable degree of correctness that the disease is frequently, if not usually, of hereditary origin, aggravated by excessive ambition and mental effort; it has a prehypertensive stage with symptoms and signs often developing as early as ten to twenty years of age, and it develops according to the plan illustrated in the chart.

Development of "Cardiovascular-renal" Disease



The blood pressure at any given time is the resultant of:

a. The condition of the heart muscle.
b. The viscosity of the blood.
c. The degree of arteriosclerosis.
d. The degree of vasoconstriction or vasodilation.

Granting the truth of these facts, treatment may be divided into prophylactic and actual.

Prophylactic.—In families in which there is a strong element of vascular disease, the parents should be told of the part played by heredity and should be urged to guide their children along the less

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strenuous walks of life and to advise them against excessive mental and physical exertion, excessive ambition, and obesity. This applies particularly to those children who show vasomotor instability and hemorrhagic tendencies early in life. It is conceivable that this disease could be almost eradicated if the marriage of the children in vascular families could be prevented. This, of course, is quite impractical, but in some cases it may be possible for parents to prevent the marriage of children from two vascular families.

Actual Treatment of Hypertension.—Given a patient with high blood pressure, the first question that arises is whether or not to treat the hypertension at all. In some mild cases it is far better not to mention the increase in blood pressure, lest the patient be made introspective about his difficulties and thereby produce a condition of increased nervous tension which would lead to greater and greater blood pressure. A tactful suggestion to the patient to slow down may be enough. The physician, however, should keep his eye on such a patient from time to time to note the rate of development of the vascular disease and to treat him when necessary. In most cases the hypertensive process must be treated because (1) the pressure is usually greater than is necessary for mere compensation, and (2) because the greater the pressure the more rapid the increase in the arteriosclerosis, and the secondary changes in the various organs.

Let me repeat what I said above—the level of the blood pressure at any given time is the resultant of the condition of the heart, the viscosity of the blood, the degree of arteriosclerosis (if any be present) and the degree of vasoconstriction or vasodilation. Which of these elements are susceptible to treatment? In our consideration of the treatment of vascular hypertension we can discard the cardiac factor because it is either a constant, requiring no therapy, or when inconstant, the condition is one of heart disease and is, therefore, outside the limits of this discussion. Viscosity of the blood may be omitted from consideration because our knowledge of this subject is extremely hypothetical. The degree of sclerosis can also be omitted because we can influence it practically none at all. The only condition that can be influenced is the degree of vasoconstriction and our treatment centers entirely around this condition. Our efforts are aimed at the reduction of excessive vasoconstriction by eliminating, as far as possible its causes. These are nervous influences, bacterial toxins and other known (guanidine, etc.) or unknown chemical substances.

The treatment of vascular hypertension starts then with a careful history to determine what systems are involved and to what extent, what is the mode of living of the patient, how many hours of sleep, how much exercise, how much relaxation, the type of work and how

many hours are spent at it, the degree of responsibility, etc. (Of course the amount of treatment and the ability of the patient to carry it out will vary with each individual.)

If it is necessary to treat the patient at all, he should be instructed to cut down on the amount of work and reduce his responsibilities and causes for worry as far as is possible. He should be urged to adopt the *laissez faire* attitude toward life. The physician should insist on frequent vacations, daily periods of relaxation with rest after each meal, particularly after the noon meal, when the patient should have a nap of one-half to one hour. In addition, he should be made to exercise if this is at all possible. The best exercise is in the form of walks, which should be graduated at the beginning, and which should never be taken immediately after meals. If the patient is unable to walk, light massage should be given as a substitute. All infectious foci with their possible vasoconstricting toxins should be eradicated, provided the strain of so doing is not too great for the patient. Bowels should be regulated so that the patient has one or two soft or liquid stools per day. The object of this is two-fold: to eliminate bacterial and chemical toxins and in addition to avoid the dangerous straining with a constipated stool. A mild saline is the best cathartic and this should be given often enough to produce the desired result. Usually twice a week is sufficient.

The diet should at all times be small in bulk with moderate restriction of protein, salt, fluid and calories. This diet aims at sparing the circulation and reducing the weight of these patients, who are usually far too heavy. If there is renal insufficiency, a diet is constructed to correspond to the degree of insufficiency. Extreme salt restriction in my hands has been of no value. (It should be remembered at all times when a remedy is tried which aims at a reduction in pressure that marked variations in pressures are the rule in this disease, and that the greatest conservatism in the interpretation of the effects of any given therapy should be exercised.)

Drugs.—These are chiefly of value to relieve symptoms.

1. The bromides are probably the most generally useful. Other sedatives, such as chloral, luminal, barbital, veratrum, etc., all may have their places. Even the opiates are at times indicated.

2. The iodides, in my experience, are of very limited value except where there is a positive Wassermann reaction. Possibly some of the organic iodides, such as lipiodin, sajodin, etc., may have greater value.

3. The drugs aimed directly at the reduction of pressures also are of little value. These include calcium chloride, alone or in conjunction with atropine, the so-called antispasmodics, such as benzyl benzoate, akineton, gui, the various nitrites, etc. The nitrites certainly

have their place in the treatment of hypertension, but such place is the symptomatic relief of angina pectoris, nocturnal smothering and cramps in the extremities.

4. Other drugs may have their special indication. Digitalis is never contraindicated by the level of the pressure, no matter how high. If the condition of the heart requires it, it should always be used. The salicylates may be of value in the headaches of hypertension. Mistletoe, especially in the form of Intrait de Gui, has a very definite place in the treatment of the headaches, vertigo and sometimes the other cerebral symptoms.

5. Other forms of therapy are occasionally indicated. A prolonged warm bath may be very soothing and produce a decreased vasoconstriction and thereby a lowered blood pressure. Turkish baths, or any form of sweat bath are fraught with considerable danger of producing cardiac overload and thereby acute pulmonary edema. Bleeding is indicated when cerebral hemorrhage or heart muscle failure threatens. Occasionally, it is of benefit in plethoric individuals who complain of various cerebral symptoms. Lumbar puncture may be of value in relieving severe headaches, mild delirium and other cerebral manifestations. The thermos bottle full of hot milk, tea or coffee is a boon to those suffering from early morning headaches and insomnia.

6. Organ extracts. Many of these have been tried from time to time, but most have been discarded. Three alone, in our present state of knowledge, have even theoretical justification. Ovarian extracts undoubtedly relieve the nervous tension in some hypertensive women who are in the menopause. The parathyroid, through its action on blood calcium, the cerebral cortex and the sympathetic system, was thought to be a possible remedy for relief of excessive vasoconstriction. Attempts by Altnow and me to influence the blood pressure with this substance have up to now proved unavailing. The liver extract is still in the process of experimentation and despite the unsatisfactory experiences of Calhoun and myself with it a year ago, we still have hopes that something will come of it. To give you the last word on its use from two sources most active in its investigation, I should like to quote from letters recently received from Dr. Major of Kansas City and Dr. MacDonald of Toronto. Dr. Major states that, "We are seeing a fall in blood pressure in about 40 per cent of our cases and relief of symptoms in from 80 per cent to 90 per cent." Dr. MacDonald writes, "In selected cases of essential hypertension, we are obtaining falls in pressure in 60 or more per cent and are obtaining relief from associated symptoms in approximately 90 per cent. In many cases the relief from symptoms is marked where no fall in pressure occurs and, as a general rule, the relief from symptoms is out of all proportion to the fall in pressure."

In conclusion, the proper treatment of a patient with high blood pressure demands an adequate knowledge of the origin and development of the hypertensive process, the interrelationship of its various parts, and the great variability in blood pressure in a given individual from minute to minute and week to week. This last indicates the necessity for the utmost conservatism in the interpretation of the effect of any given therapeutic agent. A careful history of the patient's habits and mode of living is absolutely necessary

Prophylactic treatment aims at the avoidance of the hypertensive state in the children of the so-called "vascular families" by teaching them to avoid excessive mental and physical strain and obesity.

The actual treatment of the hypertensive individual, of necessity, aims largely at the reduction of excessive vasoconstriction. This may be accomplished by a careful cutting down of mental and physical effort, by enforced periods of relaxation, by diet, by drugs and probably by the liver extract when it is perfected.

NOTE ON THE OCCURRENCE OF AN UNUSUAL FORM OF GALLOP RHYTHM

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IT SEEMS worth while to call attention to an interesting variation from the usual types of gallop rhythm which is occasionally met with but which, in the literature of the subject, has received no notice whatever. The condition, in my experience, is by no means common. I have notes upon only ten cases seen during the past fifteen years.

The phenomenon consists merely of a great exaggeration of the ordinary form of early diastolic gallop, in which the gallop sound is so loud and the corresponding palpable shock so strong as to dominate completely the cardiac signs. The sound is much louder than either of the two heart sounds which immediately precede it and is sharp and short; the shock is correspondingly sharp and quick and is readily appreciable to the eye as a quick outward rebound of a circumscribed area of the chest wall over the intercostal space where it occurs. The sound and shock resemble closely, but are even more pronounced than the first heart sound and the systolic shock in typical cases of mitral stenosis. When the phenomenon occurs in cases of mitral disease the very loud early diastolic sound adds a confusing factor to the auscultatory signs which only accurate timing will serve to identify, but when the condition has once been seen it is easily recognized thereafter.

Forms of heart disease in which it has been seen: The phenomenon has been observed in a type of disease in which the usual forms of gallop rhythm are rare. The most striking examples have been found in patients with advanced mitral disease who have entered the hospital in a state of extreme congestive heart failure, with orthopnea, cyanosis, dropsy and pulsating liver and neck veins. Four of the ten cases were of this sort. In none of these four cases was the gallop present on admission, i.e., in the stage of extreme decompensation, but after two or three days of treatment, as the patient was beginning to improve slightly, it appeared suddenly, lasted usually only two or three days and then, with further improvement under digitalis, disappeared completely. It must be this transient character, I think, that explains the fact that this striking phenomenon has not received attention. In two of these four cases, in which a relapse occurred later, there was a reappearance and then a disappearance of the gallop.

In four other cases the gallop appeared in patients with severe rheumatic fever and some valvular damage but without severe heart failure. In this second group of cases the gallop lasted from five days to two or three weeks, usually until convalescence. The ninth patient was an elderly man, seen only once, who had had a coronary thrombosis several months before, and who had had nocturnal dyspnea and Cheyne-Stokes breathing for several weeks. I had no means of telling how long his gallop had lasted. The tenth case was that of a man fifty-nine years of age who had had essential hypertension for many years, with occasional periods of decompensation for three years. It was during improvement (under digitalis) from one of these periods that the gallop became manifest. Two days later it had disappeared, with the further improvement of the patient.

Heart Rhythm.—In eight of the ten patients the rhythm was of the normal, sinus type throughout. One case had a regular rhythm at first and later a slow fibrillation, and the gallop showed no change with the transformation. In one case there was at first a regular ventricular rate of 144 per minute, with auricular flutter which under digitalis was promptly converted to a slow fibrillation, and the gallop appeared after the change.

In one case the gallop showed such an interesting relation to the occasional premature beats as to merit a detailed description:

The patient, a man of fifty-nine years, had had essential hypertension for many years and for three years had had occasional periods of decompensation. During almost the whole of this time he had had a presystolic gallop and a pulsus alternans. It was during one of these periods of failure and as he was beginning to improve, after having been kept in bed and been given digitalis, that the following note was made:

"Jan. 6, 1927: General condition improved. No liver tenderness.

Pulse has fallen to 80 and is regular except for a rare premature beat. Palpitation over apical region shows a less heaving impulse, but just within the apex beat, in the fifth space, is now felt a *very* pronounced diastolic shock. At this point are heard a faint first sound, a somewhat louder second sound and a *very* loud, sharp middiastolic sound corresponding to the diastolic shock. The intensity of this sound and shock shows distinct rhythmical variations. These variations are quite independent of changes in respiratory phase but bear a constant relation to the early, weak, premature beats which occur at intervals of from 25 to 30 normal beats. During the last 8 to 10 beats preceding each premature beat this sound becomes less and less sharp and loud and the shock becomes almost imperceptible. With the first two beats *after* the premature beat the sound and shock continue faint but with the third beat the sound suddenly becomes loud and the shock strong." During the half hour that the patient was observed this curious variation was noted with every premature beat that occurred. Three days later the middiastolic shock and sound were gone, the patient's condition was much improved and the heart showed only the familiar presystolic gallop.

Duration of Gallop.—Among the nine cases in which this point could be determined the gallop was present in two cases for only two days; in four cases it lasted for from three to seven days and in three instances, all of them from the rheumatic fever group, it persisted for two or three weeks.

Location of the Signs.—In most instances the gallop signs were confined to a very circumscribed area in the neighborhood of the apex beat but usually a centimeter or two to the right of and above the actual location of the apex. In two of the cases, however, the signs were noted as being evident in the third, fourth and fifth intercostal spaces to the left of the sternum.

COMMENT

References in the literature to this unusual form of gallop are almost completely lacking. The only detailed case on record is one published by Potain[1] in 1856. A woman forty years of age, in whom the autopsy showed an adherent pericardium, had when first seen an early diastolic shock associated with a sharp, loud sound. Later both shock and sound disappeared. Duroziez[2] describes several cases in which the early diastolic gallop sound is relatively loud and Stokes[3] refers briefly to a case with reduplication of the second heart sound in which the second part of the sound was much louder than the first. Aside from these few early notes the voluminous literature of gallop rhythm seems to contain nothing which relates to this interesting variety. It seems hardly worth while here to speculate upon the cause of these striking and peculiar signs. Since their time in the cardiac

cycle corresponds exactly with that of the normal third heart sound, it seems reasonable to suppose that they represent merely an exaggeration of the physical conditions which give rise to that normal sound. The most plausible explanation of that sound is that it is due to the sudden tension and vibration either of the mitral leaflets themselves or of the ventricular wall.

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FACTORS AFFECTING THE DISAPPEARANCE TIME OF INTRADERMAL INJECTIONS*

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THE present study was carried out with the hope of obtaining some data on the cause of edema. Aldrich and McClure[1] have shown that the disappearance time of an intradermal injection of salt solution is greatly shortened in the presence of edema. It was thought that by using different solutions for injection and by modifying the local vascular conditions, a change in the disappearance time might be effected analogous to that obtaining in edema. We were also interested in discovering if possible the fate of intradermally injected fluids, whether they were taken up by the cells, or simply diffused through the intercellular spaces.

It has usually been assumed that no bleeding should accompany an intradermal injection. In order to determine the layer of the skin where the injected material lies, we carried out intradermals upon three dead human subjects using 0.1 c.c. of a 50 per cent suspension of India ink in normal salt solution. The injected areas were then excised and sectioned. In every instance the ink was seen to lie entirely in the corium and not in the epidermis and it is inconceivable that even 0.1 c.c. could be localized in these tissues. It will be seen in the accompanying illustration (Fig. 1) that the intradermal material spreads out laterally and is sharply held below as if prevented from entering the deeper layers by a limiting membrane. The presence in the corium of intradermally in-

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jected fluids has also been emphasized by Kasahara.[2] Since the material lies in the vascular layer of the skin, bleeding at the point of injection may be expected.

THE TECHNIC

The technic used was similar to that of Aldrich and McClure. Fine needles of 27 gauge and one-half inch length were used and the volume injected was 0.1 c.c. The volume advocated by the authors quoted was 0.2 c.c. We compared 0.1 c.c. and 0.2 c.c. saline and found little difference in the disappearance time, so we adopted 0.1 c.c. as the unit for injection.

The site of injection was found to be rather an important factor in the disappearance time. At first the volar aspect of the forearm was used,

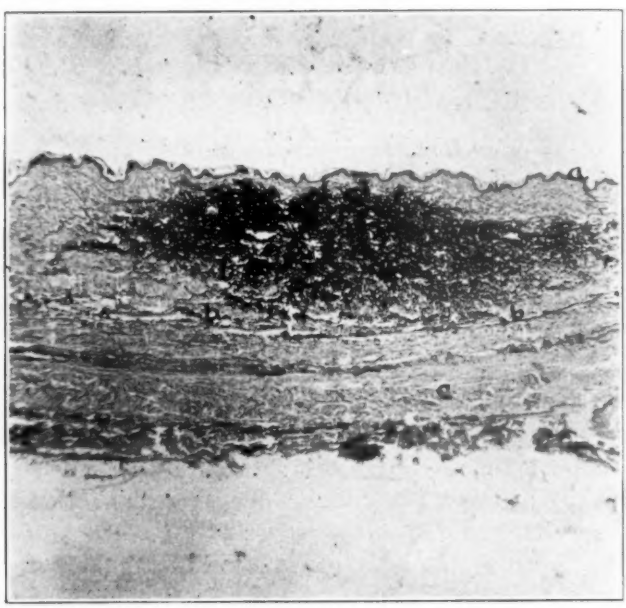

Fig. 1.—Section through an intradermal injection of India ink. *a*, epidermis; *b*, limit of penetration of injected material; *c*, subcutaneous tissues.

but it was found that the variation in disappearance time of individual injections was quite great and that those close to the elbow fold tended to disappear more rapidly than those more distally placed. It was also found that those situated close to the hair line on the lateral aspect of the forearm, usually disappeared more rapidly than those on the medial aspect, though this was not constant. The deltoid region was found to be more satisfactory and it will be seen by comparison of Figs. 2 and 3 with Figs. 4 and 5 that the results obtained were much more consistent.

The injection was made in the usual way, the "stick" being considered satisfactory if a white raised area of about 0.8 to 1.0 cm. in diameter was produced on which the hair follicles appeared as minute pits. The

time of injection of each intradermal was taken and the time was again noted when the papule could no longer be felt. In some individuals a local reaction occurred around the needle track and in those care had to be taken to distinguish the more localized indurated inflammatory area from the presence of the injected solution in the tissues. In some instances (distilled water, solutions of low P_H) this inflammatory reaction was so great that the papule remained for hours and no determination of the disappearance time could be made. During the experiments the arm of the subject was supported and kept fairly still. When comparisons were made between the disappearance time of normal salt and of any other solution, only the normal salt injections done at that time and in approximately the same area were used for comparison. This was found necessary owing to the wide variation in the disappearance time

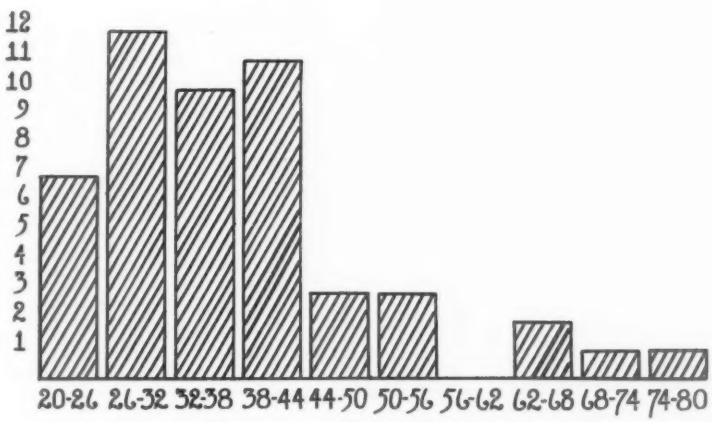

Fig. 2.—Disappearance time of normal salt in a normal subject (E. I. J.), injections into forearm. Vertical figures show number of intradermals; horizontal figures show disappearance time in minutes.

of normal salt solution at different times in the same person. The "normal salt" used was in every instance a 0.9 per cent solution of sodium chloride.

VARIATIONS IN THE DISAPPEARANCE TIME OF NORMAL SALT SOLUTION IN NORMAL INDIVIDUALS

The range of disappearance time of normal salt in any one normal individual varies within wide limits, as is shown in the accompanying figures. When the forearm is used for injection the shortest disappearance time in Fig. 2 is 21 minutes and the longest 75 minutes. In Fig. 3 the variation lay between 29 and 95 minutes. The figures for deltoid injections are less subject to variation and referring to Fig. 4 it will be seen that the time varies between 44 and 71 minutes, and in Fig. 5 between 45 and 71 minutes. Individual variations are shown on comparing Figs. 2 and 3; in the former taken from one subject the disappearance

time averages 37 minutes; in the latter from a different subject, 56 minutes. It is assumed that differences in the disappearance time in the same individual are mainly explainable by slight differences in the depth to which the salt solution is injected.

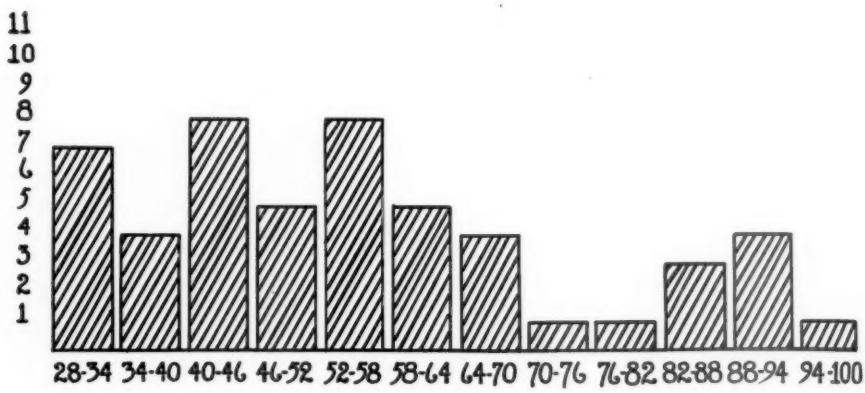

Fig. 3.—Disappearance time of normal salt in a normal subject (H. L. W.), injections into forearm. Vertical figures show number of intradermals; horizontal figures show disappearance time in minutes.

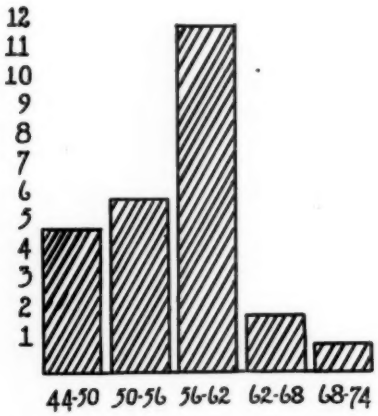

Fig. 4.—Disappearance time of normal salt in a normal subject (E. I. J.), injection into deltoid region. Vertical figures show number of intradermals; horizontal figures show disappearance time in minutes.

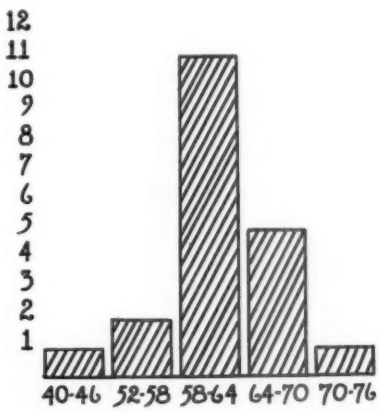

Fig. 5.—Disappearance time of normal salt in a normal subject (H. L. W.), injection into deltoid region. Vertical figures show number of intradermals; horizontal figures show disappearance time in minutes.

THE INFLUENCE OF THE AGE OF SUBJECTS ON THE DISAPPEARANCE TIME

It will be seen from Table I that age affected the disappearance time very slightly. Newborns on the whole had a shorter disappearance time than older children. The papule produced is smaller in diameter, changes color to the physiological red of the surrounding skin in a short time and is visually indistinguishable in 5 to 6 minutes. It is still definitely palpable, however.

THE INFLUENCE OF VARIATIONS IN SALT CONTENT ON THE DISAPPEARANCE TIME

It was thought that variations in the salt content might influence the disappearance time of the solution. A typical experiment is shown (Table II). It will be seen that only a slight difference is shown in this experiment—or indeed in the average of all the experiments (Table III).

TABLE I

THE AVERAGE DISAPPEARANCE TIME OF NORMAL SALT IN NORMAL SUBJECTS AT DIFFERENT AGES

AGE	AVERAGE DISAP. TIME OF EACH INDIVIDUAL				NO. OF SUBJECTS	AVERAGE FOR AGE PERIOD
	Minutes					
0- 8 days	19	33	26	33	4	28 minutes
6-12 mos.	29				1	29
1- 2 yrs.	33				1	33
7 yrs.	44	41	56	30	4	43
8 yrs.	38	35	44		3	39
9 yrs.	40				1	40
11 yrs.	52	28	48	52	4	45
13-14 yrs.	22	26	36	39	4	31
Adults	37	56			2	47

TABLE II

TYPICAL EXPERIMENT SHOWING DISAPPEARANCE TIMES OF DIFFERENT STRENGTHS OF SALT SOLUTION

NaCL PER CENT				AVERAGES MINUTES
3.6	73	79	84	79
1.8	63	77	80	73
.9	72	84	86	80
.6	?	77	77	77
.3	?	75	75	75
.0	More than 24 hours			

TABLE III

AVERAGE DISAPPEARANCE TIME OF SOLUTIONS OF VARYING SODIUM CHLORIDE CONTENT

STRENGTH OF SALT SOLUTIONS	DISAPPEARANCE TIME
3.6%	75 minutes
1.8%	61 "
.9%	47 "
.6%	62 "
.3%	66 "
Distilled water	Disappearance time not estimated

(4 subjects: 6-16 intradermal injections of each solution)

It was impossible in some instances to estimate the disappearance time of the 3.6 per cent salt and quite impossible to estimate any of the distilled water injections owing to the local inflammatory reaction which in the case of the distilled water persisted for more than 24 hours. The injection of 0.6 per cent, 0.9 per cent, and 1.8 per cent salt solution was

unaccompanied by pain while considerable pain attended the injection of the 3.6 per cent and 0.3 per cent solutions and was especially marked with distilled water. It will be seen in the figures that normal salt solution disappears somewhat more quickly than either hypertonic or hypotonic solutions and that the extremes are difficult to estimate owing to the local irritant action. The fact that the disappearance time of a hypertonic solution is no longer than that of a hypotonic solution is against the view that the disappearance of fluid is due to its being taken up by the cells.

THE INFLUENCE OF CHANGES IN P_H ON THE DISAPPEARANCE TIME

To determine if any difference existed in the disappearance time of solutions of widely differing P_H, buffers were made of KH_2PO_4 and NaOH diluted 1:5 with normal salt solution. The P_H varied in the different solutions between 5.8 and 8.0. As is shown by the table of averages (Table IV) no appreciable difference could be established in the disappearance time of these solutions. In two instances the most acid solution caused an inflammatory reaction around the needle track and no information as to the exact disappearance time could be made out.

It is, of course, impossible to decide whether or not the P_H of the cell contents is affected by changes in the P_H of the injected fluid. These observations at least demonstrate that variations in the P_H of the injected fluid, which after injection becomes a part of the interstitial fluid in the corium, do not affect the disappearance time of this fluid.

TABLE IV

AVERAGE DISAPPEARANCE TIME OF SOLUTIONS OF VARYING PH

pH	DISAPPEARANCE TIME
5.8	52 minutes
6.8	49 "
7.4	48 "
8.0	51 "
.9% sod. chloride	47 "

(16 injections of each solution: 6 subjects.)

THE EFFECT OF CHANGES IN IONS ON THE DISAPPEARANCE TIME

Ringer's solution and Ringer's solution minus calcium were injected and controlled with normal saline, the P_H of the former two solutions being 8.2. The average disappearance time for the saline was 58 minutes; for the Ringer's solution 60 minutes; for the Ringer's solution minus calcium 53 minutes. (Two subjects, 8 injections of each solution.) It is doubtful if the variation shown is in excess of the normal variations. A 1.8 per cent solution of sodium sulphate, isotonic with 0.9 per cent sodium chloride, was also compared with normal salt solution. The average disappearance time of the sulphate solution was 59 minutes, against 51 minutes, the average disappearance time of the saline

controls. (Twenty-six determinations, 5 subjects.) A slight delay is therefore present when sodium sulphate is used, but we feel this is not a significant difference, especially as the sulphate was rather irritating, and a somewhat longer disappearance time may well have been due to an inflammatory reaction.

There is considerable evidence that the permeability of cell interfaces is affected by variations in the proportion of calcium and potassium ions in the surrounding medium, calcium in general decreasing and potassium increasing the permeability. It was felt that if the disappearance of injected fluids were due to the taking up of the fluid by the cells, the facility with which this absorption proceeds should be influenced by changing the permeability of the cell boundaries. While our negative

TABLE V

THE AVERAGE DISAPPEARANCE TIME OF 50 PER CENT HUMAN SERUM IN NORMAL SALINE: AND OF ACACIA IN 5 PER CENT AND 10 PER CENT SOLUTIONS IN NORMAL SALINE

NORMAL SALINE	50% SERUM	5% ACACIA	10% ACACIA
Minutes			All present at 120 &
55	75	84*	132 minutes

(14 determinations: 4 subjects.)

*This includes only injections disappearing under 100 minutes.

results are of course not conclusive, since we have no proof that the variations in the ionic equilibrium of the injected fluids actually produced changes in membrane permeability, still the results at least do not afford any confirmatory evidence of the view that the fluid is taken up by the cell substance.

Deductions from a comparison of sulphates with chlorides rest on a firmer basis. It is well known that cell membranes in general are less permeable to sulphate than to chloride ions. If the disappearance of the injected fluid were due to imbibition of the fluid by the cell protoplasm one would expect a significantly longer disappearance time for sulphates than for chlorides. The fact that this does not take place seems to us strong evidence in favor of the view that the papule disappears merely because the fluid spreads out through the intercellular spaces until its boundary is no longer distinguishable.

THE EFFECT OF CHANGES IN VISCOSITY ON THE DISAPPEARANCE TIME

To determine the effect of viscosity of injected substances on the disappearance time, two substances were used. One was a 50 per cent solution of human blood serum in normal salt solution. The other was acacia in 5 per cent and 10 per cent solution in normal saline. The P_H of the latter was found to be quite low, so that it was necessary to adjust it to about 7.6 before injection. From Table V it will be seen that the disappearance time was greatly lengthened by the addition of serum and acacia to the solutions.

TABLE VI

COMPARISON OF DISAPPEARANCE TIME OF 5% ACACIA AND 5% ACACIA IN 1:1,000,000 ADRENALIN

SOLUTION	DISAPPEARANCE TIME				AVERAGE
	Minutes	Present at	Present at	Present at	Present at	
Acacia 5%	96 96 60	96 minutes	95 minutes	110 minutes	120 minutes	?
Acacia 5% in Adrenalin	29 37 25	28	40	40		33

(13 Injections: 3 normal subjects.)

THE EFFECT OF THE ADDITION OF ADRENALIN ON THE DISAPPEARANCE TIME

Adrenalin diluted 1:1,000,000 in normal saline was injected intradermally. Blanching of the papule and the occasional appearance of the pseudopodial blanched areas were observed. It was found that the average disappearance time for the adrenalin solution was 27 minutes as against 45 minutes, the time taken by the salt controls. (Thirty-one injections; six subjects.) The same experiment on a rabbit showed an average disappearance time of 48 minutes for the normal salt solution and 29 minutes for the adrenalin. On a dog the normal salt solution took an average of 100 minutes, against 75 minutes for the adrenalin (6 determinations of each). Further observations were made in a few cases, comparing the disappearance times of 5 per cent acacia in normal saline and 5 per cent acacia in 1:1,000,000 adrenalin in normal saline. Here again the results were striking, as shown in Table VI.

The experiment was done with the view of deciding the possible influence of vasoconstriction on the disappearance time of the salt solution. The more rapid absorption rate was quite unexpected.

THE EFFECT OF HEAT AND COLD ON THE DISAPPEARANCE TIME

The effect of heat.—Intradermal injections of normal saline were done on both forearms. One arm was immersed in a water-bath kept between 45° and 46° C., the other serving as a control. (Five subjects, 21 injections.) The average disappearance time on a heated arm was 47 minutes; for the control side 50 minutes—insufficient difference to warrant the conclusion that the increased blood flow altered the disappearance time.

The effect of cold.—The technic was similar to that described above, except that the water was kept at about 9.5° to 10° C. On both arms the disappearance time was 43 minutes.

(Twenty determinations; 5 subjects.)

The effect of local cold.—An intradermal of normal salt was done on each arm. On one side the papule was kept cold by the light application of small pieces of ice. On the control side the papule disappeared after 39 minutes; but the intradermal to which ice was applied was still distinctly palpable after 1 hour, and was red in color and surrounded by a red areola.

TABLE VII

THE DISAPPEARANCE TIME OF NORMAL SALINE WITH CHANGES IN BLOOD FLOW AND VENOUS AND CAPILLARY PRESSURE

SUBJECT	WITHIN 10 MM. OF SYSTOLIC PRESSURE MINUTES	CONTROL	AT LEVEL OF THE DIASTOLIC PRESSURE MINUTES	CONTROL	AT LEVEL OF HALF DIASTOLIC PRESSURE MINUTES	CONTROL
H. L. W.	48	45			30	50
	29	33	45	52	42	35
E. I. J.	42	41	38	35	34	34
M. B.	18	15	26	24	20	19
M. J. P.	41	45				
Averages	36	36	36	37	34	35

THE EFFECT OF CHANGES IN THE CAPILLARY AND VENOUS PRESSURE AND VOLUME FLOW ON THE DISAPPEARANCE TIME

In the following experiments intradermal saline injections were made on both forearms and the venous pressure of one side raised with the cuff of a sphygmomanometer, the other arm serving as a control. Three levels of pressure were taken on each individual on separate occasions, four subjects being used in this experiment. The results were as follows: (1) with the venous pressure raised to a point at or within 10 mm. of the systolic blood pressure, the average disappearance time on that arm was 36 minutes, and on the control arm 36 minutes; (2) with the venous pressure raised to the level of the diastolic the average disappearance time was found to be 31 minutes, the control being 37 minutes; (3) with the venous pressure raised to one-half the diastolic pressure the figures were respectively 34 and 35 minutes. There was, therefore, no appreciable difference when the arterial supply was practically cut off and no difference when the venous pressure was considerably increased. It has been shown by Drury and Jones[3] that raising the venous pressure to between 40 and 80 mm. Hg. will result in the production of palpable edema after a varying length of time. An increase in limb volume due to the presence of edema occurs even after 10 minutes.

Thus in our experiments slight edema must have been present yet without any decrease in disappearance time. The individual averages are shown in Table VII.

To discover if a longer lasting impairment of the arterial supply would affect the disappearance time, the femoral artery of a dog was ligated on one side; the other side being used as a control. During the 7 days of observation no appreciable disability resulted from this operation. On the seventh day the dog was killed; it was found that the ligation was below the profunda femoris. The blood supply was thus not completely obliterated but presumably was considerably diminished.

It will be seen from Table VIII that no difference in disappearance time on the two sides was observed although great daily variations oc-

curred. These variations are difficult to explain especially as intradermal injections in dogs are sharply defined and the end point easy to determine.

TO FIND THE RATE OF ABSORPTION AND EXCRETION OF PHENOLSULPHONEPHTHALEIN WHEN INJECTED INTRADERMALLY

Phenol red was made up so that 0.5 c.c. of a solution contained 6 mg. of the dye. The P_H was brought to 7.4 by the addition of NaOH. Two of the intradermals disappeared within 2 hours of injection. The others

TABLE VIII

DISAPPEARANCE TIME OF INTRADERMALLY INJECTED SALINE AFTER LIGATION OF FEMORAL ARTERY IN A DOG

(Daily averages given.)

	1ST DAY POSTOP. MINUTES	2ND DAY POSTOP. MINUTES	4TH DAY POSTOP. MINUTES	7TH DAY POSTOP. MINUTES
Rt. leg (ligated)	37	20	35	95
Left leg (control)	37	40	29	96

showed a local inflammatory reaction, some of the dye remaining for several days. The dye appeared in the urine within 15 minutes and after 2 hours 65 per cent had been excreted. With this rapid excretion it was probable that some of the injected water has also entered the circulation although as has been shown the amount so removed does not appreciably

TABLE IX

DISAPPEARANCE TIME OF NORMAL SALINE INJECTED POSTMORTEM IN HUMAN SUBJECTS

NO.	SUBJECT	AGE	ANTE-MORTEM DISAP. TIME	TIME ELAPSING BETWEEN DEATH & POST-MORTEM INTRADERMAL	DISAPPEARANCE TIME OF INDIVIDUAL INTRADERMALS	AVERAGE	NOTES
			Minutes		Minutes	Minutes	
1	E. S.	6 yr.		3 hr.	172	172	
2	D. W.	9 mo.		12 hr.	45— 65	55	Slight terminal edema
3	H. O.	18 mo.		3 hr.	180—180	180	
4	J. L.	7 mo.	20	2 hr.	35— 40	38	
5	E. C.	Adult		12 hr.	70—180	125	
6	C. M.	2 mo.	29	30 minutes	15— 18	17	Slight edema
7	F. P.	9 yr.	30	18 hr.	45— 40	43	

Average of all postmortem intradermals—83 minutes.

affect the disappearance time of the papule. The rate of excretion of phenolsulphonephthalein when injected intradermally into rabbits has been studied by Kasahara.[2] He found that excretion was only slightly slower than when the injection was made subcutaneously and that after 20 minutes a variable amount could be detected in the urine.

THE DISAPPEARANCE TIME OF INTRADERMAL SALT SOLUTION INJECTED POSTMORTEM

It has been stated by Olmsted[9] that intradermal salt solution disappears as quickly postmortem as antemortem. Injections were carried out in a series of 7 subjects at varying lengths of time postmortem. The disappearance times are shown in Table IX. The average disappearance time was 83 minutes, showing a definite prolongation over the antemortem figures. In only one subject was the disappearance time shortened and no terminal edema was present to afford a possible explanation of the difference.

DISCUSSION

The results obtained with adrenalin, heat and cold and compressing pressure around the arm are unfortunately quite difficult of interpretation. With adrenalin two effects are known to be produced, a great local diminution in blood supply and a local acidosis.[4] The more rapid disappearance with a diminished blood flow apparently means that removal of the injected fluid by the blood stream is playing hardly any part in the disappearance of the papule. One cannot suppose, however, that the fluid has merely been taken up by the cells in situ: water would occupy the same volume inside a cell or out and a protoplasmic imbibition into the cells at the injection site could not make for rapid and complete disappearance of the papule. This, it seems to us, rules out what at first thought might appear to be an explanation of the rapid disappearance with adrenalin; namely an increased acidity of the cells in the injected area. Further evidence against acid being a factor is the failure of a more rapid disappearance when acid solutions are injected.

It seems then that the fluid disappears merely by spreading out into the surrounding region of the corium and perhaps also into the underlying tissues. Adrenalin was the only factor which decreased the disappearance time and it is not at all clear why the presence of adrenalin in the injected fluid should produce a simulation of the conditions obtaining in edema. An increase in blood flow by immersion of the arm in hot water did not affect the disappearance time. It is true that the blood flow to the control arm is also increased[4] but not nearly to the same extent as in the immersed arm. Immersion in cold water produces no change in disappearance time. Here we do not know that the blood flow through the immersed arm is any different than that through the control arm, since the flow to both is cut down greatly. If, however, we compare all the cold results with all the heat results we find practically no difference in the disappearance times under the two conditions. This shows clearly that great variations in blood flow can take place without appreciably affecting the disappearance time. Both Stewart[5] and Hewlett with Van Zwaluwenburg[6] have shown that a change of several hun-

dred per cent in the volume flow to the arm would result from such changes of temperature as are employed and there is no doubt that the skin circulation is participating in these changes to at least as great an extent as that of the other arm tissues.

According to Stewart[7] application of a cuff encircling the arm at a pressure of 15 mm. Hg below systolic practically abolishes the blood flow through the forearm. At a cuff pressure 25 mm. below systolic the blood flow is only a small fraction of normal. With a cuff pressure 10 mm. below diastolic the blood flow is in the neighborhood of one-half normal. At a pressure of one-half the diastolic the blood flow is unimpeded. Our experiments with compressing pressures on the arm were done with the idea of seeing if changes in the blood flow and capillary and venous pressure so produced would change the disappearance time. The failure of any change to occur was unexpected in view of reports of a decreased disappearance time in regions where the blood flow was diminished by various pathological conditions.[8] The absence of any decrease in disappearance time when edema was artificially produced by cuff pressure was also unexpected. It suggests that the edema so produced is not akin to the edema which occurs in those pathological conditions where a decreased disappearance time is noted. The normal disappearance time in the absence of a circulation confirms our conclusion that the removal of fluid by the blood stream is an insignificant factor in bringing about a disappearance of the papule. Since there is also an "outlying acidosis," these experiments are further confirmation of the conclusion that changes in acidity do not affect the disappearance times and our supposition that the fluid merely diffuses out is strengthened. These experiments then have ruled out certain factors which might be supposed to cause a decrease in disappearance time. They have not shown what the effective factor is in edema.

SUMMARY

1. Intradermally injected fluid lies in the corium.

2. There are rather wide variations in the disappearance time of intradermal injections made:

(a) In different regions in one and the same normal subject.

(b) At different times in a restricted area in one and the same subject.

(c) In different normal adult subjects.

3. The disappearance time of 0.1 c.c. normal salt solution is practically the same as that of 0.2 c.c.

4. Variations in acidity of injected fluid or of tissue at the site of injection do not affect the disappearance time.

5. The disappearance time is not significantly affected by variations in osmotic pressure, hydrogen-ion concentration, or potassium-calcium balance of injected fluid nor by substituting sulphate for chloride ions.

6. The disappearance time is greatly lengthened by increasing the viscosity of the injected fluid and greatly diminished by the addition of adrenalin.

7. Variations in the blood flow through or changes in the capillary and venous pressure at the site of injection, do not affect the disappearance time under the conditions of our experiments.

8. The local application of cold to the site of injection increased the disappearance time.

9. Phenol red injected intradermally appears in the urine within 15 minutes, 65 per cent being excreted within 2 hours.

10. The disappearance time postmortem is usually longer than antemortem.

11. The removal of fluid by the blood stream is not a significant factor in determining the disappearance time. We believe that the disappearance of the papule is due merely to the spreading out of the fluid intercellularly. We do not know what the factors are which accelerate this process in edema.

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STUDIES ON THE VISCERAL NERVOUS SYSTEM

XVIII. Reflexes from the Peritoneal Viscera to the Heart*

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IT IS well known that gastrointestinal "upsets" in some way produce, or contribute to the production of, cardiac irregularities, especially when the heart is already diseased. The mechanism by which the "upset" affects the heart is not clear. Some state that the cardiac irregularities are due to the absorption of toxins, others that they are due to the pressure of an overdistended colon against the diaphragm, thus encroaching upon the space of the thoracic cavity, and still others that they are of vagus reflex origin or a combination of reflex activity plus toxic impairment of the myocardium. Mackenzie states, ". . . indiscretions in food and drink may readily induce these extrasystoles." He suggests no mechanism but elsewhere[1] he writes, ". . . it may produce flatulent distention of the stomach and bowels, which, pressing upon the diaphragm embarrasses the heart and respiration." Romberg[2] states that these "upsets" may start extrasystoles mechanically. Muns[3] cites a very interesting case of paroxysmal tachycardia. The patient in his youth experienced relief from the attacks by soapsuds enemas. Later in life the attacks became refractory to medical treatment. Removal of a chronic appendix gave him complete relief from the attacks for several months. Mild attacks then returned, but they were controlled by digitalis. Hamburger[4] has recently had a similar experience in the case of a young girl. Here is good presumptive evidence of a reflex mechanism producing, or contributing to the production of, the irregularity. Sauerbruch states,[5] "Operations in the neighborhood of the heart may produce arrhythmia or following low blood pressure, paroxysmal tachycardia." He indicates that these irregularities may be due to direct stimulation of the vagus and sympathetic nerves to the heart. Hamburger[6] gives an excellent general statement of the problem particularly from the point of view of the cardiac irregularities associated with gall bladder disease. He cites also the pertinent literature: Umber,[7] tachycardia, irregularities, brachycardia due to gall bladder pain; Hoppe-Seyler,[8] pulse irregularities of vagal origin from gallstone colic. Straus[9] states, "While it is generally agreed that extrasystoles . . . are due to conditions of abnormal irritability, in the cases I have to report, this increased local irritability may have been the result of, or at least

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initiated by, a reflex stimulation from the vagus-supplied viscus (gall bladder), or due to the absorption of toxins from the pathologic organ reaching the heart and rendering it abnormally irritable, or both combined." Straus and Hamburger[9] report two cases showing complete disappearance of extrasystoles following cholecystectomy. Hewlett[10] states, "Vagus slowing of the heart may also be due to reflexes that

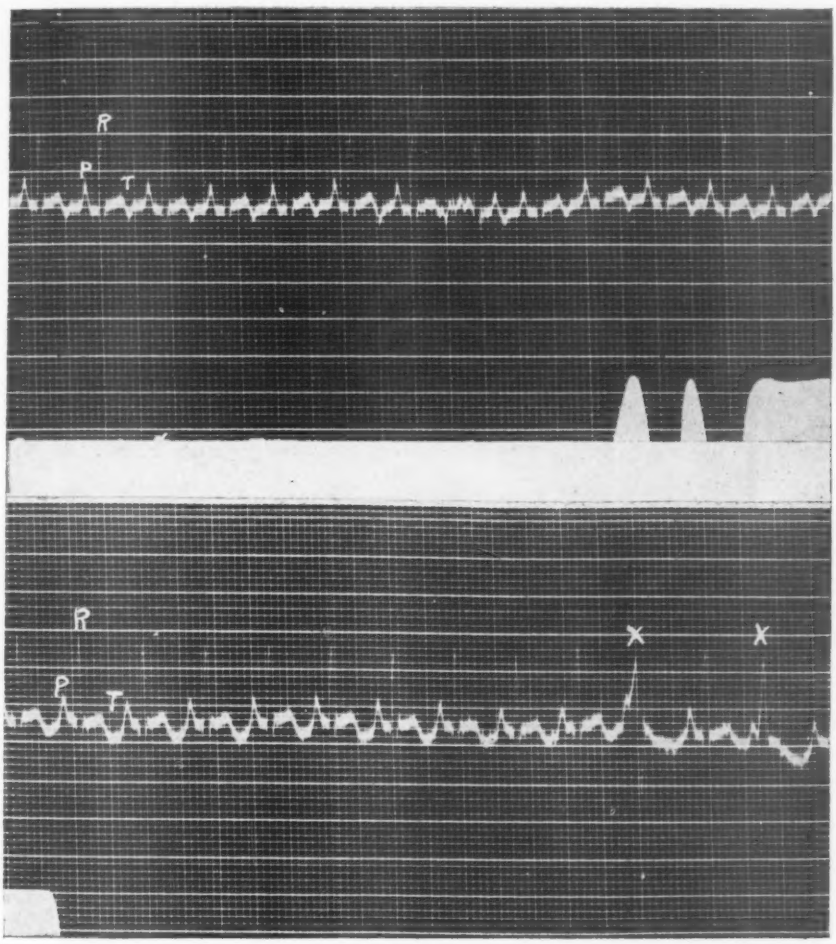

Fig. 1.—Two strips of electrocardiogram showing the effect of barium chloride on the T-wave. The T-wave increased in negativity from −0.1 m.v. to −0.2 m.v. and increased in duration from 0.06 sec. to 0.12 sec. The interval R to end of T increases from 0.20 sec. to 0.26 sec. The first two extrasystoles ("x") produced by the drug are also shown. The white band at the bottom of the record indicates the injection of the barium chloride. The second strip does not follow the first immediately.

arise from the nose, the eyeballs, or the abdominal organs." T. I. Bennett[11] writes, "In patients with organic disease of the heart, gastric dilatation from aerophagy may be productive of the most serious consequences. Palpitation, tachycardia, or cardiac irregularities may

occur, but it is possible by this means to produce much more formidable conditions, such as an attack of true angina pectoris, or cardiac collapse." Sir W. Bennett[12] cites this case: During the removal of a tumor from the rectovaginal septum attacks of distressing tachycardia developed. They persisted until the stitches were removed. They then disappeared. They were apparently reflex in origin.

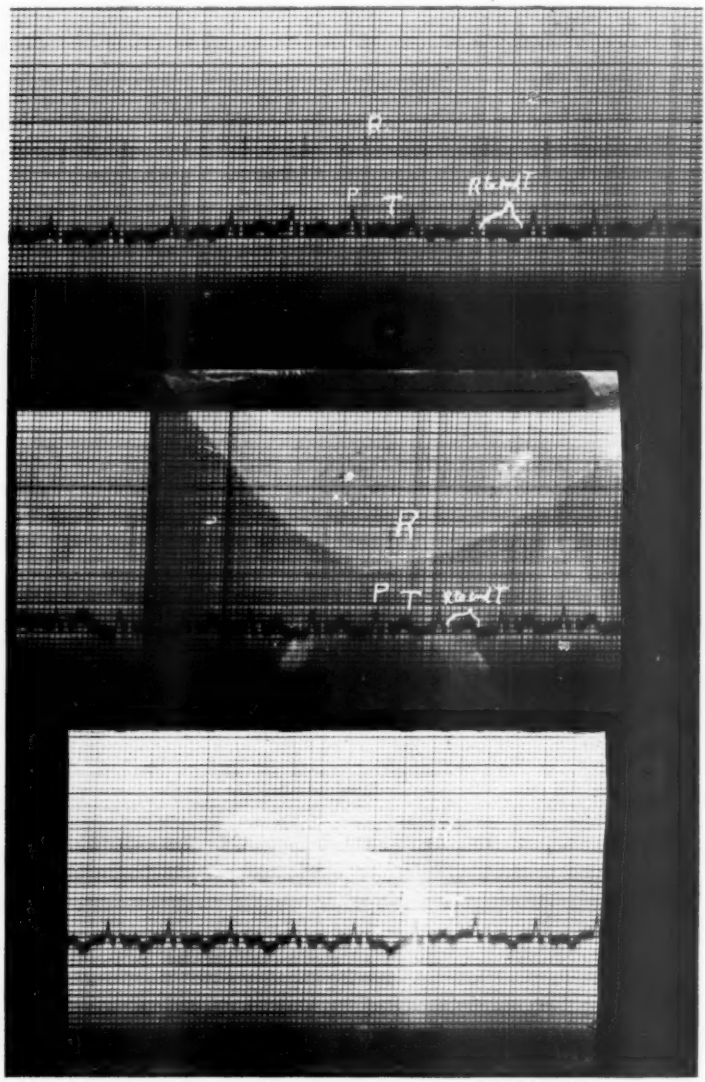

Fig. 2.—Three strips of electrocardiogram illustrating the increase in voltage of T resulting from stimulation of the abdominal viscera. The upper and lower strips are the normal records which were taken before and after stimulation. The middle strip was taken during stimulation of the parietal peritoneum (by rubbing it with the finger tips). The interval R to end of T decreases from 0.28 sec. to 0.22 sec. and returns to 0.27 sec. after stimulation. The height of T increases from +0.1 m.v. to +0.15 m.v. The strips do not follow one another immediately.

Extrasystolic irregularities were early considered due to abnormal activities of the extrinsic nerves. It was a gratuitous assumption without any experimental evidence. Under the usual conditions of experimentation stimulation of the extrinsic nerves does not produce extrasystolic irregularities. Furthermore, these irregularities can be

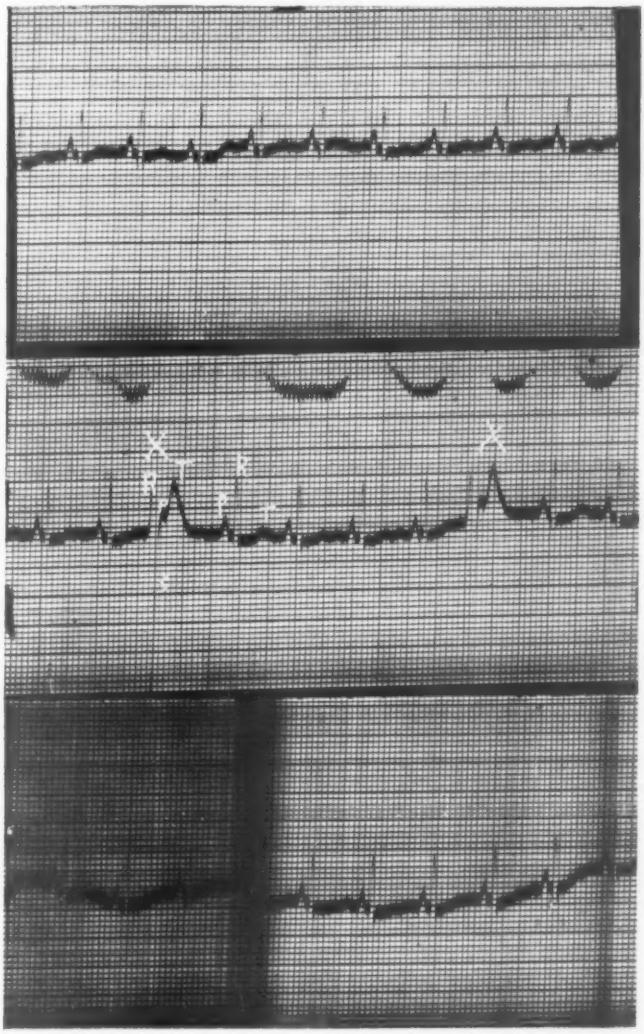

Fig. 3.—Three strips of electrocardiogram, from Lead III illustrating the production of extrasystoles by stimulation of the abdominal viscera. The upper and lower strips are normal records which were taken before and after stimulation respectively. The middle strip was taken during distention of the small intestine. Two left ventricular extrasystoles ("x") are shown. Barium chloride had been administered previously and the vagi were cut. The strips are noncontinuous.

produced in the isolated perfused heart and by various drugs as $CHCl_3$, etc.[13] Therefore, the extrinsic nerve hypothesis was in ill repute and practically forgotten.

It has been known[14] for years that vagus stimulation could cause a heart to fibrillate when the auricular conditions were "set" but that ordinarily it would not do so. Rothberger and Winterberg,[15] in 1911, reported extrasystolic irregularities from combined vagus and sympathetic stimulation. As Lewis[16] points out, "It is becoming clearer that when nerve stimulation produces extrasystoles, paroxysm, or fibrillation, the chamber affected is in some way predisposed." Rothberger and Winterberg[17] have shown that after small doses of barium chloride, sympathetic stimulation will produce these disturbances.

In 1924, at the time our[18] work on this problem was begun, the facts seemed to be that (a) direct nerve stimulation of the heart, when it was previously prepared by disease or poisoning, produced irregularities of the heart beat and that (b) treatment of an intestinal "upset" or surgical removal of an inflamed peritoneal organ, such as the appendix or gall bladder, occasionally caused heart irregularities to disappear. But there never had been any indisputable *proof* that cardiac irregularities could be produced reflexly.

EXPERIMENTAL METHODS

Barbitalized dogs were used. The technic was essentially that described by Tatum.[19, 20] The animals under barbital were connected with a large model (Equipment No. 1) Hindle Electrocardiograph. The abdomen was opened by a linea alba incision and a balloon placed in the viscus to be studied. A dilute solution of barium chloride was then slowly injected intravenously until the first appearance of irregularity. The actual amount injected varied considerably in different dogs. The average dose needed was from two to eight milligrams. After the cessation of the extrasystoles, the record was closely watched for any tardy extrasystoles. When after several minutes, no extrasystoles occurred the viscus was gently distended. In repeating the experiment, it was necessary to inject nearly as much barium chloride as before. The second dose averaged from one-half to four milligrams. These procedures could be repeated several times with consistent results.

Digitalis was used in other experiments because of its frequent use clinically and because, by its use, much longer normal periods were obtainable. When barium chloride is used, the heart is in suitable condition for the reflex production of irregularities for only fifteen to twenty minutes. With digitalis this period is extended to from three to six times this length of time. A hypodermic preparation of digitalis was injected until the first irregularity appeared. If the injection had been slow enough, that is over one-half an hour or more, the irregularities ceased after from one to ten minutes. Observation of the "string" movements and photographic record then showed no irregularity for one-half hour. The viscus being studied was then stimulated. A series of premature contractions occurred. After the cessa-

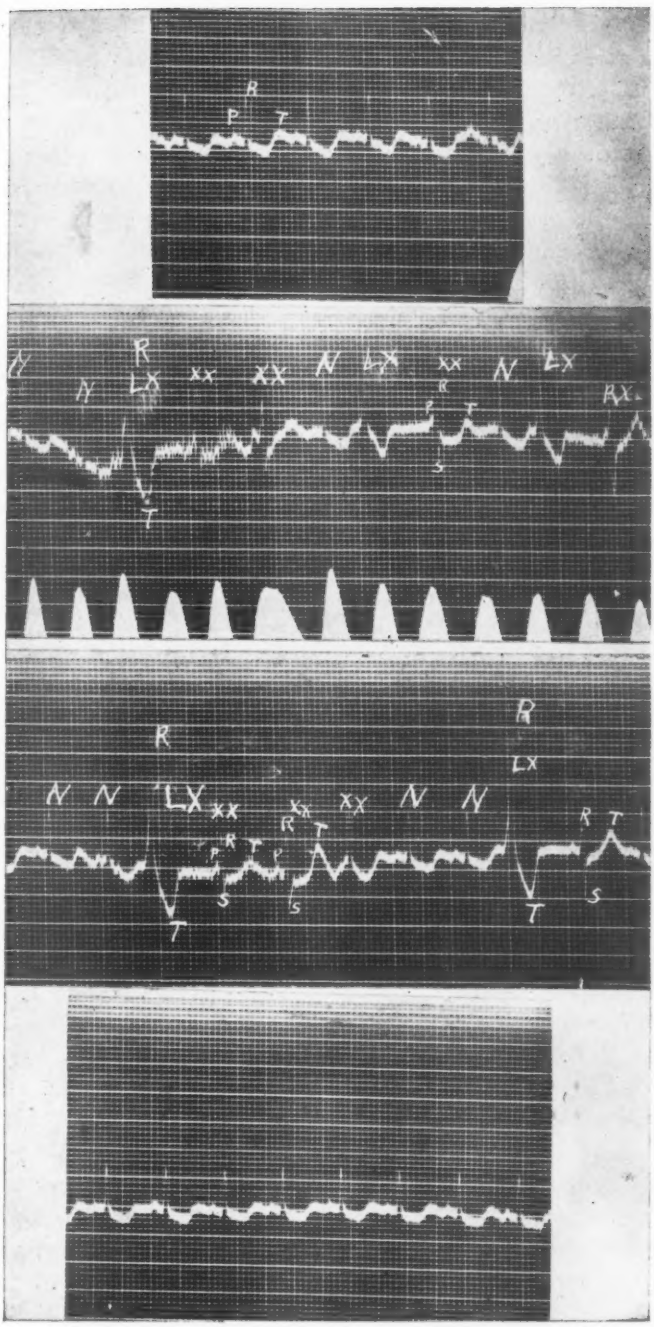

Fig. 4.—Four strips of electrocardiogram, from Lead I, illustrating more pronounced reflex cardiac effects from stimulation of abdominal viscera. The vagi were both cut and digitalis had been administered twenty minutes previously. The extrasystoles produced by digitalis had ceased ten minutes previously. The first and fourth strips are normal records taken before and after stimulation respectively. The second strip was taken during, and the third strip immediately after, vigorous mechanical stimulation of the testes. The chief response was left ventricular extrasystoles ("LX"), although there were some right ventricular extrasystoles ("RX") and some aberrant forms ("XX"). In the third strip normal curves are increasingly evident.

tion of the stimulation the irregularities stopped within from one-half to several minutes, depending upon the intensity and duration of the stimulation. No further irregularities occurred until the stimulation was repeated, after which, the results were exactly the same as those occurring during and following the first stimulation. We were thus able to repeat the observation several times following the first single injection of the drug. Thus, the possibility of the occurrence of occasional tardy irregularities due to the drug alone could not complicate the results. After the first series of irregularities following the digitalis injection, absolutely no irregularities occurred except coincident with or immediately following stimulation of a viscus. The irregularities of the heart, therefore, must have been due to the reflex from the stimulated viscus acting upon the drugged heart. When the intestine was to be distended, it was first placed outside the abdominal wall to eliminate the possibility of the distention producing direct pressure effects upon the diaphragm.

RESULTS

Since this is an electrocardiographic study, the results will be stated in electrocardiographic terms.

Auricle.—The P-wave was not altered. The P-R and the R-R intervals were not changed. Therefore, no alteration which was referable to the auricle was observed. This result is consistent with the failure to find any evidence of vagal activity resulting from visceral stimulation, for, of course, vagal activity is manifested chiefly by the auricles. Had the visceral stimulation changed the vagal tonus or activity the P-wave, the P-R interval, or the R-R interval would have been altered.

Ventricular complex.—The T-wave was greatly varied by the drugs. It is well known[21] that digitalis produces inversion of the T-wave. The action of barium chloride was even more dramatic. A typical instance is shown in Fig. 1. The T becomes markedly more negative and the negative phase widens out from 0.06 to 0.12 sec., so that the interval R to end of T increases from 0.20 sec. to 0.26 sec. The appearance of the first extrasystoles from the drug are also shown. Stimulation of the peritoneal viscera caused the T to become more positive as shown in Fig. 2. The interval R to end of T decreases from 0.28 sec. to 0.22 sec., returning to 0.27 sec. after the cessation of the stimulation. The effect of stimulation on the T, therefore, was exactly opposite to that of the barium chloride. The effect was the same whether one distended the gall bladder, the small intestine, the colon, the urinary bladder, the uterus, squeezed the testis, or irritated the parietal peritoneum. In the conscious human also we found that barium chloride and distention of the gut produced similar changes in the T-wave and R to end of T interval.

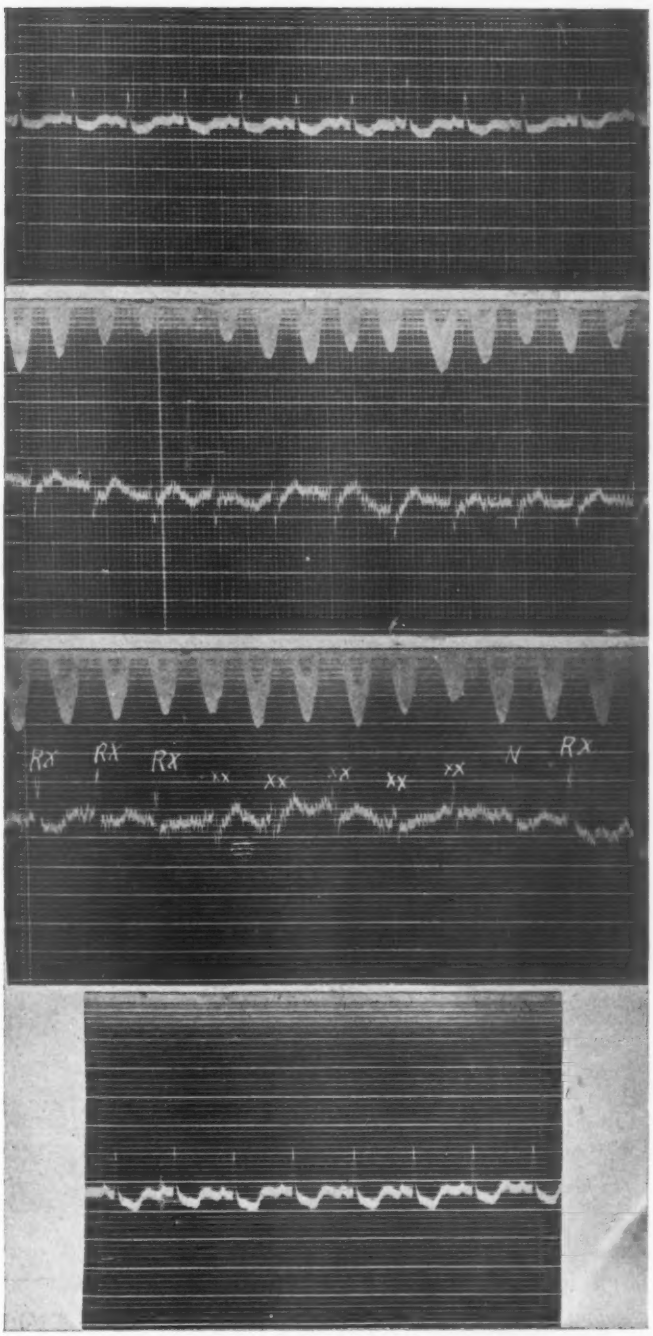

Fig. 5.—Four strips of electrocardiogram taken ten minutes after those shown in Fig. 4, without administration of additional digitalis. There was a long period of normal beats previous to the first strip. The first and last strips are of normal records which were taken before and after stimulation respectively. The second and third strips were taken during stimulation of the parietal peritoneum by rubbing with the finger tips. The second strip shows a very regular series of atypical left ventricular extrasystoles (see text). The third strip shows four right ventricular extrasystoles and a number of transition, or aberrant forms.

Stimulation of any of the abdominal tissues mentioned will also produce ventricular extrasystoles. We were never able to obtain extrasystoles without first introducing cardiotoxic doses of barium chloride or digitalis. Even when these drugs were used, it required considerable care to get the heart and nervous system into just the appropriate conditions before we were able to get results. When we followed the proper precautions, however, we were able to obtain constant results in practically every animal used, the variations being no greater than those observed in experiments on other complicated reflex mechanisms. Fig. 3 shows the response from moderate distention of the small intestine after administration of barium chloride and after double vagotomy, typical left ventricular extrasystoles (Lead III) with the P-wave on the upstroke of the extrasystolic T and the usual compensatory pause.

Fig. 4 shows a greater reflex response. This is from Lead I. It resulted from mechanically stimulating the testes twenty minutes after administration of digitalis. The vagi were cut. In addition to typical left ventricular extrasystoles and an occasional right ventricular extrasystole aberrant complexes are prominent. Fig. 5 (Lead III) is from the same experiment ten minutes later, without further administration of digitalis. It was obtained by rubbing the parietal peritoneum with the finger tips. Marked aberration is seen, in addition to the showers of left ventricular extrasystoles followed by occasional right ventricular extrasystoles (extrasystoles despite the regular rhythm because: (1) they are independent of P waves; (2) the chief deflection, R or S is opposed to the final deflection; (3) the chief deflections increase in duration from 0.03 sec. to 0.07 sec., and (4) the chief deflections increase in amplitude).

There was no parallelism between the change in the T and the development of irregularities in either the case of drug action alone or of drug action plus visceral stimulation. Premature contractions resulted in some cases in slight change in the T whereas in other cases marked change in the T was unaccompanied by premature contractions.

The R-R interval, or heart rate, was not affected by visceral stimulation regardless of whether the vagi were intact or cut. In dogs, under ether or barbital anesthesia or decerebrate and without anesthesia, we have never been able to alter the heart rate by stimulation of the abdominal viscera.

We[18] have been able to alter the amplitude of both auricle and ventricle by visceral stimulation, but as it was not demonstrable electrocardiographically it will be reported fully in a later paper with other reflexes from the viscera affecting blood pressure, blood flow, and blood distribution.

The cardiac irregularities were obtained in all cases equally well and identically whether the vagi were intact or severed. When the

vagi were intact and the cord was cut so as to eliminate the sympathetic system from participating in the reflex, the irregularities were never observed. It is certain, therefore, that the cardiac irregularities are due to the "sympathetic reflexes" (plus preliminary cardiac poisoning) and are not due to reflexes over the vagus nerves.

We[20] have shown in other experiments that the afferent nerves from the stimulated organs which are involved in these reflexes enter the spinal cord at approximately the segments observed by Head,[22] whose studies were made on referred pain from these organs in man.

CONCLUSIONS

Stimulation of abdominal viscera produces reflex sympathetic activity of the heart. In the normal animal and in man[23] this sympathetic activity is not detectable electrocardiographically. When the heart is poisoned by drugs, such as barium chloride or digitalis, this sympathetic activity is manifested electrocardiographically by elevation of the T and decrease in the R to end of T interval.

The sympathetic activity is also manifested by premature contractions of the ventricles, and by various degrees of aberration. These cardiac disturbances are certainly due to sympathetic activity because the vagi were cut, and they could not be produced when the sympathetics were cut while the vagi were intact. It is known[24] that either sympathetic stimulation or epinephrin makes T more positive. Furthermore, Rothberger and Winterberg[15] have obtained premature contractions by sympathetic stimulation after poisoning the heart with barium chloride in dosages similar to those used by us.

The nervous pathways for reflexes in man and dog are practically always the same. Without reasonable doubt, cardiac disturbances of the kind herein mentioned arise in man clinically from stimulation of abdominal viscera, as in gall bladder disease and in chronic appendicitis. The reflex pathway is over the visceral afferent nerves to the cord and over the sympathetic efferent nerves to the heart.

The only possible mechanism of cardiac disturbance from the abdominal cavity not discussed is that of direct pressure being transmitted through the diaphragm to the heart and great vessels of the thoracic cavity. That greatly increased abdominal pressure in man would not produce cardiac disturbances even in diseased hearts was shown[23] at the Cook County Hospital in 1925. Sufficient air was forced into the intestinal tract via the rectum to produce very marked difficulty in breathing without producing the slightest detectable cardiac disturbance.

SUMMARY

1. In dogs under barbital anesthesia, with both vagi either severed or intact, after the intravenous administration of the appropriate dosage of barium chloride or digitalis, stimulation of the abdominal

viscera produced disorders of the heart beat as recorded electrocardiographically.

The stimulation was (a) moderate distention of the gall bladder, the small intestine, the colon, or the uterus; or (b) mechanical squeezing of the testes, or any of the organs in (a); or (c) gentle rubbing of the parietal peritoneum with the finger tips.

2. The cardiac irregularities observed were: (a) elevation of the T-wave and decrease in the interval R to end of T; (b) premature contractions of either ventricle (usually the left), or occasionally, premature contractions of the bicardiogram type.

3. Proof is given that these disorders are due only to increased sympathetic activity on the heart when the heart is previously injured by certain drugs or poisons.

4. It is pointed out that such cardiac disorders probably occur clinically from diseased abdominal viscera by the mechanisms listed above.

5. In barbital anesthetized dogs and in the conscious human individual barium chloride depresses the T-wave and increases the interval R to end of T. In the human, as in the dog, intestinal distention produces reflex elevation of the T-wave with corresponding decrease in the interval R to end of T.

We acknowledge with pleasure our obligations to Professor A. J. Carlson and Dr. Walter W. Hamburger for such generous criticism and unfailing inspiration as make research possible.

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A CLINICAL INTERPRETATION OF PULSE PRESSURE*

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ABOUT twenty years ago the sphygmomanometer was added to the physician's armamentarium, thus enabling him to measure the blood pressure with considerable accuracy. But with this instrument of precision, as with other mechanical aids to diagnosis, the perfection of technical methods to measure deviations from the norm has outstripped our ability to interpret correctly the meaning of these deviations. This has seemed to be particularly true regarding the deviations of blood pressure from the accepted standards.

The clinical observations reported here are submitted as further evidence supporting the conception that a relationship exists between pulse pressure and ventricular systolic output.

The idea that the pulse pressure varies directly with the stroke volume is not new. Erlanger and Hooker[1] in 1904, after extensive experimental studies, suggested that the velocity of blood flow could be represented by the product of pulse rate and pulse pressure. Two years later, von Recklinghausen[2] showed that with normal arterial elasticity the pulse pressure varies with the systolic output per beat. More recently Wiggers[3] concludes from the experimental work of himself and others that "although there is a general correspondence between amplitude of pulse pressure and the output of the heart . . . in the sense that both increase and decrease synchronously so that the course of one may be prophesied from the other . . . there is no quantitative relation."

But, clinically, we are seldom concerned with exact quantitative measurements although the proper interpretation of deviations from the norm is of the utmost importance for correct diagnosis and prognosis. In this connection I wish first to show the result of one thousand observations of the relation of pulse pressure and pulse rate to basal metabolic rate.

It is frequently stated that the blood pressure is elevated in the various forms of Graves' disease though the relation between blood

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pressure and the elevated metabolic rate, which characterizes these conditions, is not generally recognized.

It will be observed from Fig. 1 that pulse rate and systolic pressure both increase gradually as the metabolic rate becomes higher, but that the diastolic pressure remains at practically the same level.

It is generally admitted that the increase in pulse rate serves, in part at least, the purpose of augmenting the volume flow of blood, which augmentation is necessary in order to carry the larger volumes of oxygen consumed. But the associated alterations in blood pressure

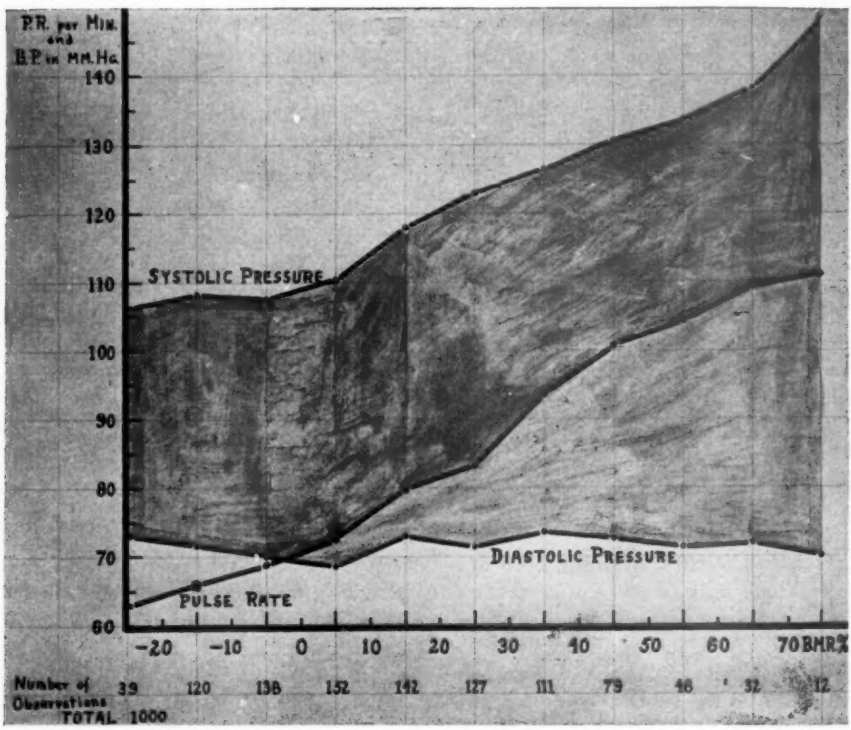

Fig. 1.—The average basal systolic and diastolic blood pressures and pulse rates as determined with the basal metabolic rate. Although the average systolic pressure and pulse rate increase as the metabolic rate becomes higher, the diastolic pressure shows no change. The shaded area indicates the pulse pressure.

are not so easy of explanation. With the diastolic pressure practically constant it seems logical to assume that the elevated systolic pressure is really a result of an increased pulse pressure and that a wide pulse pressure is in some way helpful in maintaining an augmented minute volume. The circulatory changes found in toxic thyroid disease are the same as those occurring in exercise. Both conditions are characterized by the consumption of larger volumes of oxygen which the blood is called upon to transport. This is accomplished chiefly by increasing the output of blood per minute and only slightly by removing

a greater per cent of oxygen from the hemoglobin in its transit through the capillaries. Davis, Meakins, and Sands[4] conclude from their studies of blood flow in hyperthyroidism that, "The minute volume output of the heart is increased in proportion to the increase in metabolism, the two being closely correlated." These workers also confirm observations of Plesch[5] that the minute volume is augmented by increasing the stroke volume as well as the heart rate.

I submit the observations recorded here as evidence in support of the conception that the wide pulse pressure observed in most thyrotoxic patients with elevated metabolic rate is indicative of increased systolic output and that the higher the metabolic rate the greater the pulse pressure. This veiwpoint places a physiological rather than pathological interpretation upon the high systolic pressure of thyrotoxicosis when it is accompanied by a normal or low diastolic pressure. And that the diastolic pressure is usually low is borne out by inspection of the published blood pressure readings of other investigators. Dameshek[6] reports that in 141 cases the average diastolic pressure was 72.5 mm. of Hg. with the systolic averaging 146 mm.

The normal or low diastolic pressure observed here speaks for little peripheral resistance; furthermore peripheral dilatation is evidenced by the well-known signs of flushing, sweating, warm skin, and capillary pulse found in hyperthyroidism. These factors permit a free return of blood to the heart with opportunity for rapid and complete filling of the left ventricle even in the shortened diastole. The slight or moderate cardiac enlargement, usually without signs of congestive failure, also speaks for complete filling of the ventricle, since the size of the heart seems largely determined by its content of blood.

In another entirely different condition there occurs a similar deviation of blood pressure from the norm which I believe is a physiological adaptation to compensate for a pathological condition in the heart. I refer to the blood pressure in those individuals with heart-block who are not incapacitated by the slow pulse. One occasionally sees such individuals, usually by accident, and they present a most unusual circulatory adaptation. Obviously such patients can maintain an adequate tissue nutrition only by increasing the output per beat, or abstracting more than the usual one-third of the oxygen from the circulating blood. Since there is no evidence that this latter mechanism is resorted to, it is interesting to inquire into the blood pressure readings in these subjects.

It was my good fortune to see two such individuals within the past year. Neither was suffering from any circulatory embarrassment. One came under my observation because the slow pulse had aroused the curiosity of an intern who asked me to take an electrocardiogram of the man, and the other was sent to me because in a routine examination the systolic blood pressure was found to be 180 mm. of Hg.

CASE 1.—Male, aged seventy-six years. Had known for many years that his pulse was slow. No symptoms of circulatory insufficiency. Able to earn a living for himself and wife. Often walks from the first to the fourth floor of the office building where he works, without dyspnea, though he says his legs get tired. States his feet never swell. Pulse accelerates six to eight beats per minute on exercise.

I first saw him June 21, 1926. Blood pressure, 200/70. Electrocardiogram showed complete heart-block. Auricular rate 62, ventricular 30.

On March 12, 1927, I went to his office to see him and was able to corroborate his story as to physical fitness. Examination showed a stockily built man, weighing 170 pounds. Complexion very ruddy. Pulse rate, 38-39; blood pressure, 174/72. No edema of ankles or other signs of inadequate circulation. Systolic murmur at apex and aortic area; thickening of vessels not noticeable. Pulse slow, very forceful and full; the systole seemed to be prolonged, and there was a feeling of considerable power behind the arterial wave.

Fluoroscopic examination of the heart showed a definite double diastolic distention of the left ventricle. There was also a double outline in the teleroentgenogram, measurement of which revealed a heart size at the upper limit of normal. The unusual roentgen finding of the double ventricular shadow and double diastolic enlargement may be interpreted as indicating that the ventricle is filled twice during the long diastole, the auriculoventricular ratio being almost two to one.

CASE 2.—Female, aged forty-seven years. When six years old she had diphtheria during an epidemic in which three of five children in the family died. Shortly after this she says she turned very blue when surf-bathing. She has known that she had a very slow pulse since her teens when she was taken to a physican for some other irrelevant complaint. She says at the age of twenty she could dance all night and now suffers no restriction of activity as she walks, rows, swims and plays golf without dyspnea or other signs of circulatory embarrassment. She took an anesthetic at twenty-five years for childbirth.

I first saw her July 28, 1926. Pulse rate, 39; after exercise, 44 per minute. Blood pressure, 180/80. Electrocardiogram revealed a complete heart-block; auricular rate, 60; ventricular, 40.

Physical examination showed good color, no edema. Systolic murmur at apex on expiration; also at pulmonic area. When taking the blood pressure there was a suggestion of alternation in the force of the beats; also on auscultation there was noted a difference in the quality of every alternate beat.

She was seen again on April 13, 1927, and reported she had enjoyed her usual good health during the intervening nine months. The pulse rate was 39-41 and there was still the definite alternation in the force of the heartbeat. Careful study of the blood pressure, reading the systolic pressure by palpation and auscultation, revealed that every alternate contraction raised the pressure to 170-174 mm., while the intermediate contractions registered only 144-150 mm. The diastolic pressure was 74 mm.

It seems probable that the phenomenon of alternation in this case may result from different volumes of blood expelled by the ventricle at alternate contractions. Since the auricle contracts three times to two contractions of the ventricle, the contractions may be so synchronized that during one diastole the ventricle receives two fillings from the auricle, while during the following diastole the auricle contracts but once.

A teleroentgenogram in this case also showed the heart to be at the very upper limits of normal.

COMMENT

The interesting feature of both these cases is the manifest circulatory efficiency in the presence of complete heart-block, together with high systolic but normal diastolic pressures, giving a pulse pressure of

102 to 130 mm. in one and 70 to 100 mm. in the other case. It seems to me that with a normal diastolic pressure and no evident arteriosclerosis, the elevation of systolic pressure may be simply the result of increased pulse pressure, which I interpret as indicating a larger stroke volume.

Most recorded cases of complete auriculoventricular dissociation are of patients with concomitant myocardial damage which puts restrictions upon physical activity. But individuals like the two here reported are occasionally seen and present illustrations of the power of adaptability possessed by the circulatory system. Mackenzie and Wenckebach have commented upon such cases and Thomas Lewis[7] has the following to say:

> Fullness of pulse and high systolic pressure (170-200 mm.) consequently characterize the arterial system when in persistent heart-block there is no lack of healthy cardiac tissue. In evidence of the adaptability which the circulation as a whole shows to the new conditions, I may cite the case of a patient, in whom, judging from the signs and symptoms, the damage to the muscle mass was but little. The patient, a man of 33 years, was known to have a heart rate of 30-35 with occasional accelerations to 48 for 15 years. He was the subject of complete heart-block. There was a little hypertrophy of the heart but no subjective symptoms. He led, when last seen, a very active business life, and, passed in the street, would have been judged a perfectly healthy person. There was no circulatory embarrassment even after strenuous exercise. He prided himself upon his sprinting power and had recently run in the races.

When Lewis mentions specifically the high systolic pressure in compensated heart-block, we may assume that he has found the diastolic pressure normal and we are led to the belief that increased pulse pressure is the usual finding in this condition. In seeking further data on this point I was assisted by Dr. W. J. Kerr, of the University of California Medical School, who has made some studies of heart-block. His records showed systolic pressures ranging from 130 to 220 mm. (mean, 167) with diastolic pressures from 45 to 90 mm. (mean, 70) giving a mean pulse pressure of 97 mm. The age range in these patients was from fifty-five to eighty-five years and the point may be raised that heart-block is a disease of late life and the blood pressure changes are due to arteriosclerosis.

But the hypertension of arteriosclerosis is usually marked by an elevation of diastolic as well as of systolic pressure, the pulse pressure being about one-half of the diastolic and one-third of the systolic pressure, while the myocardium remains competent to carry the increased load.

One would not expect arteriosclerosis to be a factor in elevating the systolic pressure in children and young people with heart-block, but in the few cases of juvenile block in which the blood pressure is recorded an increase in pulse pressure is noted, although the diastolic pressure is low. One child of eleven years in Dr. Kerr's series, with

complete block and pulse rate of 44, had a blood pressure of 110/55. In the Stanford heart clinic is the record of an eighteen-year-old girl with complete heart-block, pulse rate 45, blood pressure 150/96; and also a seventeen-year-old boy, with pulse rate 47, blood pressure 130/65.

It would seem therefore that arterial thickening is not the factor leading to the high systolic pressure which seems to be so constantly present in heart-block, especially when compensation is maintained.

The observations reported here are clinical and the deductions purely inferential that pulse pressure is an approximate measure of systolic cardiac output, though there is accurate experimental work supporting the inference. Lundsgaard[8] studied the blood flow in two patients with complete block and found that the stroke volume was increased from a normal of 80 to 155 c.c. with the pulse rate almost half the normal (36-41.) He gives only the systolic pressure (175 mm.) in his one uncomplicated case.

A bit of evidence indicating that these blood pressure changes are adaptive and occur quickly with the advent of block was found in the record of a case studied by Carter and Dieuaide.[9] Their patient had a heart rate of 68 with normal sinus rhythm and blood pressure of 130 mm. systolic and 85 mm. diastolic, but the next day with complete block the values were 128 mm. systolic and 60 mm. diastolic with heart rate of 20 per minute. This gives an increase in pulse pressure of 23 mm. of Hg. during block. On the third day when sinus rhythm was again restored the blood pressure returned to its former levels. Their patient, like the two reported here, showed no signs of circulatory embarrassment during the periods of block nor did he suffer limitation of activity. This observation, together with other studies made, led these authors to conclude that the "respiratory and clinical data suggest that the resting ventricular output must have increased in the presence of heart-block almost in proportion to the fall in rate."

SUMMARY

In summary I will say that the minute volume of the heart, being the product of heart rate and stroke volume, may be varied by altering either one or both of these factors; augmented blood flow results from an increase in one or both, and diminished flow follows a decrease in one or both. Proportionate changes in both but in opposite directions tend to maintain a constant minute volume. I have shown that in certain conditions alterations in pulse pressure occur which are in the same direction as one would expect stroke volume to vary in these conditions. While pulse pressure is not a measure of systolic output, its direction and magnitude of variation seem to parallel the changes in output.

This is illustrated by the known circulatory changes in elevated metabolism, whether in exercise or diseased states. Augmentation of minute volume here is usually effected by increasing heart rate and stroke volume. The blood pressure findings which characterize this state are normal diastolic and wide pulse pressure, resulting in elevated systolic pressure.

When an adequate minute volume is maintained in the presence of a very slow pulse resulting from heart-block, the systolic output per beat is increased. The blood pressure alterations in this instance are marked elevation of systolic with normal or lowered diastolic pressure.

These clinical observations suggest that the physiological significance of elevated pulse pressure, with normal diastolic pressure, is increased stroke volume.

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CARDIAC ANEURYSMS*

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ANEURYSMS of the heart are of interest mainly to pathologists. They are, for the most part, beyond the reach of treatment and are rarely recognized during life. However, the dependence of parietal aneurysm upon myomalacia cordis may justify suspicion of aneurysm in a few instances where coronary thrombosis with infarction has been previously diagnosed.

My interest in aneurysm of the heart was aroused by a patient who contracted bronchopneumonia while at work as a laborer and died suddenly on the fourth day of the disease. Autopsy revealed a rather extensive parietal bulging of the apical region of the heart with rupture and extravasation of blood into the pericardium. The anterior descending branch of the left coronary artery was tremendously thickened and narrowed in that portion of its course which was proximal to the fibrous sac. The patient gave no history of previous cardiac disease, and necropsy unexpectedly revealed the aneurysm above described with rupture of the heart as the cause of death.

This experience stimulated me to assemble the records and material of cardiac aneurysms which have come under observation at the Stanford Medical School. Five such cases have been studied and followed to autopsy. In none was an antemortem diagnosis of cardiac aneurysm suspected. One, possibly two, had symptoms suggesting a previous cardiac infarction, and three, of the ordinary senile failing heart of hypertensive arteriosclerotic type. In one the possibility of syphilitic myocardial change was considered. A study of this small group impresses one with the abrupt and increasing severity of myocardial insufficiency when cardiac infarction presumably occurred rather than the recognized symptom complex of coronary thrombosis with precordial pain as the outstanding feature. (See recapitulation of case reports and comments as noted below.)

Except in congenital cases, cardiac aneurysm is dependent for the most part upon coronary arterial disease. The left coronary is the more important, being the vessel more likely to become occluded. It runs in the left ventricular groove to supply the anterior wall of the left ventricle, the anterior papillary muscle and the left half of the thickness of the interventricular septum. Its circumflex branch turns posteriorly in the auriculoventricular groove, supplying the posterior

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wall of the left auricle and of the left ventricle, the posterior papillary muscle, and part of the septum. The right coronary artery runs along the right or posterior interventricular groove and supplies the right ventricle over its main extent. Its circumflex branch continues forward around the right side of the heart, supplying the right auricle. (For detailed description of the blood supply of the heart, see Gross.[1])

The end artery theory of Cohnheim has successively been modified. That anastomoses do exist between the capillaries of the coronaries has been quite definitely established not only by experimental ligation in animals and by clinical observation with autopsy dissection, but also by the use of injections of dye preparations and finally, after injection, by corrosion of the extravascular tissues in both normal and diseased hearts. Roentgenological studies, after corrosion of the extravascular tissues, demonstrate conclusively the precapillary anastomosis between the two coronary arteries by the escape of metallic mercury after injection from the opposite coronary artery under 125-150 mm. pressure. (See Oberhelman and LeCount.[2]) (For early investigation regarding the collateral anastomoses of the coronary arteries, see the experimental and pathological reports by Cohnheim, and Schulthess-Rechberg,[3] Porter,[4, 5] Hirsch,[6] Merkel,[7] Spalteholz.[8, 9])

Assuming a sizable collateral capillary bed in cardiac tissue, a part of the heart wall rather less in extent than the area supplied by a ligated or thrombosed artery dies and promptly assumes the character of an anemic infarct. The size of such an area of infarction depends upon the size of the occluded vessel, the anatomical anastomosis of the adjacent branches, the condition of the heart musculature, and the patency of the outlying vessels at the periphery of such an area.

These variations are well exemplified by the experimental work of Smith,[10, 11] who ligated various branches of the coronaries in dogs and studied the subsequent pathological effect. In brief, his studies led him to conclude:

(a) The pathological lesion resulting from the ligation of the ramus descendens anterior is fairly constant in type but varies widely in the extent of involvement of the heart wall. In six hearts the ventricular wall at the apex was reduced almost to paper thickness with beginning aneurysm.

(b) The pathological findings resulting from ligation of the ramus circumflexus sinister were most surprising in that the external changes were comparatively small.

(c) The lesion resulting from the ligation of the right coronary artery was confined to the lateral and anterior surface of the right ventricle about the size of a silver dollar, and small areas of fibrosis disseminated in the right auricle.

Experimental evidence of early aneurysm is thus cited, because it agrees closely with histopathological material studied at autopsy. Such material has shown that the degree of myomalacia cordis varies tremendously according to the arterial branch occluded, but in the main, thrombosis of the left anterior descending artery produces an

effect which is fairly constant in the size and position of the area of infarction if this vessel is occluded near its point of origin.

Clinical and pathological study has also shown that aneurysm of the heart wall is preceded by a focal degeneration of the cardiac muscle, which, in the majority of instances, is caused by arteriosclerosis of a coronary artery with subsequent thrombosis of a sizable branch of the coronary artery. While thickening of the vessel wall may be extreme without obvious symptomatology, such narrowing can be quickly completed by the formation of a thrombus upon a degenerative plaque, thereby obstructing the flow of blood except by the inadequate anastomosis of the adjacent vessels of the heart wall. Depending upon the size of the occluded vessel such an area of anemic infarction may occupy a large part of the ventricular wall or interventricular septum. A large or small area of infarction can heal completely into a somewhat thin fibrous scar which replaces muscle. A large area of this type which yields to intracardiac pressures gives rise to a parietal bulging, which, if extreme, constitutes a cardiac aneurysm.

A large area of infarction commonly becomes lined with thrombi and pericardial adhesions are generally found on its surface. These adhesions often limit accurately the area of infarction or aneurysm.

Aneurysm of the heart is usually located in the left ventricle in the proximity of the apex. It is rare that the shape of such an aneurysm resembles that so commonly seen in the large arteries. It is usually not visible externally and appears as a depression hollowed out at the expense of the thickness of the heart wall. Only rarely is the boundary between the healthy muscle and the seat of the aneurysm sufficiently distinct that the sac projects from the ventricle, thereby changing the outline of the heart. The bulging is lined by stretched endocardium which is at times greatly thickened. Laminated blood clot usually fills such a pouch if the process has progressed, or, if such a process be early, thrombotic masses often adhere to the endocardial surface. (See articles on cardiac aneurysm by Pelvet,[12] Thurnam,[13] Legg,[14] Hall,[15] Kahn,[16] Elliott,[17] Bourland,[43] Lutembacher,[44] Strauch.[49])

Aneurysms of the auricles, valves or coronary arteries per se, have at times been reported, but are of the rarest occurrence. Cases like the two of Ingram and MacFie,[18, 19] are quite unusual, that of aneurysm of the anterior cusp of the mitral valve being probably on a basis of syphilis.

Aneurysm of the undefended space is probably of congenital origin, as Mall has shown. As a result of a misplaced inferior septum, the membranous septum develops improperly and becomes placed in a horizontal and not in a perpendicular position. In such a position it is weakened in every way, and this predisposes to the formation of aneurysm. Sacculations, either single or multiple, of the membranous portion of the septum project into the right auricle above the medial

cusp of the tricuspid, and in some cases extend also into the musculature of the interventricular septum. At times the medial cusp of the tricuspid valve is involved in this process as in the case of MacCallum,[50] and also of Mall.[51]

Syphilis of the heart assumes in no way the paramount rôle that spirochetal infection plays in the production of aneurysm of the aorta. To be sure, one can demonstrate at times in the heart muscle, as in the aorta, distinct gummatous formation and obliteration of the vessels supplying these parts, but specific arterial disease apparently plays a greater part in localized weakening of the heart wall than does the inflammatory reaction of gummatous formation. When syphilitic changes take place in the intima of the coronary branches, thrombosis may as readily take place as in nonspecific arteritis with plaque formation (Case 1, Robinson and Herrmann[20]). MacCallum[21] says: "Aneurysmal dilatations of the apical region of the left ventricle of the heart have been considered of luetic origin in many cases, all stages being demonstrable between the fresh gumma of the septum and the wall of the heart and the distended scarred sac." The hearts of both congenital and acquired syphilitics have been described which show, besides fresh gummas of the heart wall, aneurysm of the ventricle, or, aneurysm of the septum in conjunction with syphilitic aortitis and positive blood reaction. (See case reports Friedlander and Isaacs,[22] Young,[23] Ingram and MacFie,[19] and many others.)

A septic embolus lodging in a coronary vessel and resulting in myocardial abscess may be a very occasional cause of cardiac aneurysm if such an abscess be extensive enough to materially weaken a sizable area of the heart wall. The more frequent location of such a lesion is around the aortic valves and adjacent tissue. (See McCarthy.[24]) Focal degeneration coincident with or immediately following severe infection which consists in part of edema, fibrinous coagula, leucocytes, and hyaline degeneration, weakens the cardiac muscle as a whole. The same may be said of the less acute focalized areas of acute rheumatic fever, i.e., Aschoff bodies. Neither condition produces localized muscle weakness of sufficient extent to allow of bulging from intracardiac pressure.

The sequence of events which result in myomalacia cordis substantiates the dependence of aneurysm of the heart wall upon coronary arterial disease. Postmortem study commits the ramus decendens anterior as playing the major rôle in aneurysm of the left ventricle. The constancy of the findings in experimental ligation of this same branch in the dog's heart, impresses one with the tremendous importance of this artery in coronary thrombosis with subsequent ventricular bulging.

The symptomatology of cardiac infarction has been recently stressed by many authors. "In the main, the symptoms of aneurysms of the heart are not otherwise distinctive from the symptoms of the cardio-

vascular disease in the course of which the aneurysm develops." (Kahn.[16]) When, therefore, symptoms of coronary thrombosis are diagnosed, myocardial degeneration and thinning of a portion of the ventricular wall should be suspected. Assuming that coronary sclerosis precedes infarction, a history of previous attacks of angina pectoris is given by a certain group. In five out of seven cases of cardiac aneurysm reported by Cabot,[25] either angina pectoris or symptoms suggesting cardiac infarction or both, were present.

In general, a history of coronary thrombosis is of extreme importance. Such a condition may manifest itself by acute and persisting severe pain over the precordia or upper mid abdomen (Osler,[45] Allbutt,[26] MacKenzie,[27] Libman,[46] Willius,[48] Herrick,[29, 30] Gordinier,[47] White[31]), which is unrelieved by vasodilators, rest, or posture. Dyspnea is often present and the face is anxious and shows at times extreme pallor. The systolic blood pressure falls, and a localized friction rub is often heard over a portion of the cardiac area. Such a patient may or may not give a precedent history of myocardial insufficiency, but in those individuals with signs and symptoms of a decompensated heart muscle, the onset of coronary infarction, according to Wearn,[32] is apt to cause a sudden increase in these signs and symptoms. Many cases of cardiac aneurysm have been followed from the time of suspected coronary thrombosis until autopsy revealed the final diagnosis. Many of these had fairly typical attacks of pain as above described, while in the group reported below, the outstanding feature in the majority is a sudden increase in the signs and symptoms of a decompensated heart muscle. There is no doubt that in cardiac aneurysm, pain is far from constant, being often absent. Sometimes pain, as Sternberg[33] has shown, may be associated with a patch of pericarditis.

Irregularities of the heartbeat caused by the sudden shock of an occluded coronary seem in no way diagnostic of the condition. Possibly paroxysmal tachycardia of ventricular origin, ventricular extrasystoles and alternation of the pulse are the most important. (Kahn,[16, 34] Robinson and Herrmann,[20] and others.) Experimental occlusion of the branches of the coronary arteries shows variable results. Numerous irregularities, such as extrasystoles, tachycardia, auricular fibrillation, auricular flutter, and ventricular fibrillation may occur. (Smith,[10, 11] Robinson and Herrmann.[20]) Interventricular aneurysm with heart-block has been reported as part of a syphilitic process of the heart and aorta by Friedlander and Isaacs.[22]

When a large branch of a coronary artery becomes suddenly occluded, stoppage of the heart may be almost instantaneous, or death may follow within a few minutes. In an analysis of eighty-six cases of coronary sclerosis by Willius and Brown,[35] 71 per cent of the sudden deaths occurred in patients with infarction of the myocardium.

LeCount's[36] conclusion from a study of twenty-six cases of coronary occlusion is to the point, in that, although collateral anastomoses exist between the coronary arteries and those of the adjacent structures, yet with sclerosis or with more acutely developing obstruction from other causes, the compensatory circulation may prove inadequate or may not be established promptly enough to prevent sudden death. From an experimental and clinical point of view, it is remarkable how much damage certain cardiac muscles can withstand before evidence of stoppage or of gradual failure becomes manifest. Miller and Matthews,[37] in experimentation on dogs, found that only 8.7 per cent of the animals died after ligation of the left circumflex and none after ligation of the left descendens 10 mm. or less from the orifice. Examination showed that the ligature was always below the branch given off to the septum. This work was carefully controlled and supercedes the work of Cohnheim, Porter, and others. Autopsy experience goes to prove that human beings can often withstand extensive occlusion of the coronary arteries, for it is not uncommon to find large infarctions revealed only by death from their rupture or from some other cause.

Electrocardiographic signs of coronary thrombosis are important. Both clinical and experimental reports (Herrick,[30] Kahn,[34] Pardee,[39] Pardee and Master,[38] Willius,[28, 40] Robinson and Herrmann,[20] Smith[10, 11, 41]) in a measure confirm the change in the electrocardiogram. Smith's work with ligation of branches of the left coronary artery gave fairly constant results in that the T-wave frequently became inverted in Leads I and II after twenty-four hours. He observed a change from a strongly positive peak immediately following ligation, and the height that it assumed apparently depended upon the degree to which the circulation to the left ventricle was disturbed. From the strongly positive peak the T-wave swung to a markedly negative phase and then a slower return to the positive or isoelectric form. After the fourth week, however, the T-wave again became isoelectric or negative in one or more leads and remained so until necropsy. Herrick, Kahn, Pardee and Master, report clinical cases of coronary thrombosis, verified by autopsy, in which there was inversion of the T-wave in Lead I or in Leads I and II. According to Willius, T-wave negativity results from alternation in potential distribution from changes in contraction preponderance. According to Kahn, when changes involve the special fibers of conduction a certain degree of blockage to the conduction current takes place in the ventricular muscle. This is manifest as an increase in the QRS complex and low voltage with preponderance of the left ventricle. The progression of these electrocardiographic features with inversion of the T-wave in Lead I is illustrated in two cases (Kahn[16]). In one the anterior descending branch of the left coronary was thrombosed with resultant change in the myocardium, in that the apex region was transformed

into connective tissue and was "thinned to blotting paper." Such studies are of decided importance in the diagnosis of cardiac infarction with subsequent aneurysm formation.

Roentgen-ray studies, from the very nature of the gentle bulge of the heart wall, are in no way distinctive of this condition; only under the rarest conditions does an abrupt change occur in the contour of the heart wall enough to arouse suspicion of cardiac aneurysm by irregularity in the outline of the left border of the heart. (Smith,[42] Case 1.)

The cases herein reported have been reviewed from the records of the hospital. It is unfortunate that full data such as radiologic study, electrocardiographic study and specific history referable to cardiac infarction are not in all cases available.

CASE 1.—M. H., female, aged seventy years, German. Patient had been in comparatively good health up to the time of the present illness. This dated from a period six weeks previous to admission. At this time patient began to feel weak and became breathless on exertion. Slight swelling was subsequently noticed in the feet and ankles. These symptoms progressively increased, and on admission, September, 1914, orthopnea and nocturnal dypsnea were marked, and the abdomen was distended with fluid. There was history of sharp and persistent precordial pain. The heart was enlarged to the left and downwards; a soft systolic murmur was noted over the precordium; no friction rub was heard. Rhythm—fibrillation. The lungs showed evidences of passive congestion; the liver was enlarged and tender; signs of ascitic fluid were noted in the abdomen. The urine contained albumin and casts; blood Wassermann was negative. Patient progressively failed and expired suddenly twelve days after admission.

POSTMORTEM DIAGNOSIS BY DR. OPHULS

1. Arteriosclerosis—general—with cardiac hypertrophy.
2. Arteriosclerosis—local—coronary, with large scars in left ventricle.
3. Thrombosis of right auricle.
4. Embolism of pulmonary artery.
5. Embolism of splenic artery with infarction.
6. Aneurysm of heart.

Heart: Specifically the right heart showed moderate dilatation and hypertrophy. Right ventricle was fairly firm and the wall averaged about 4 mm. in thickness. Small laminated thrombus in auricular appendage on right side. In the region of the apex of the heart, there was slight aneurysmic dilatation of the right ventricle about 5 cm. in diameter. Marked dilatation of the left auricle and even more marked of the left ventricle, the wall of which was hypertrophied and averaged 15 mm. Lower half of the system and of the anterior wall of the left ventricle and entire apex was replaced by dense fibrous tissue about 5 mm. thick and somewhat distended. Left coronary artery showed a marked arteriosclerosis and was completely obstructed about 4 cm. from its origin. The right coronary showed less arteriosclerosis; no obstruction. There were numerous small white scars in the lower part of the hypertrophied muscle. Valves on the left side showed a few slight yellow thickenings.

Base of aorta showed a slight irregular thickening of the intima and a few small arteriosclerotic plaques just above the sinus of Valsalva.

Kidneys: There was a marked arteriosclerosis of the left renal artery, the capsule was slightly thickened and the surface was slightly granular and showed several large deep retracted scars. The right kidney showed only slight granulation on the surface and no large scars. The branches of the renal artery on both sides showed marked thickening.

CASE 2.—E. A. J., female, aged seventy-five years, American. Patient entered the hospital in January, 1915 in a semicomatose condition. The complaint of agonizing pain, radiating from the chest into the upper abdomen, back of neck, and left shoulder was obtained. This pain remained fairly constant for two days but was tremendously aggravated on the third day until morphine was given for relief. Examination revealed a patient somewhat irrational. The heart showed no enlargement but the sounds were distant. No murmurs were heard. The pulses were synchronous, regular, and not rapid; systolic pressure 110 mm.; moderate general arteriosclerosis noted. The lung bases showed diffuse crepitant râles. The liver and spleen were not palpable; no ascitic fluid was noted; no edema of the extremities. Patient remained in the hospital for a month, during which time her cardiac condition showed some improvement. She was catheterized for a pyelitis, and after the successful passage of the catheter, the patient gave a sharp cry and passed away suddenly.

POSTMORTEM DIAGNOSIS BY DR. OPHULS

1. Arteriosclerosis—general.
2. Arteriosclerosis—local—of the coronaries.
3. Aneurysm at the apex of the heart.
4. Heart, rupture of (spontaneous).

Heart: Specifically the pericardium contained about 350 c.c. of fluid blood and partly recent clot. At the apex of the heart there was an old adhesion between the apex and pericardium about 5 cm. in diameter. Heart was a little below normal size; right auricle and right ventricle were normal size; wall of the right ventricle showed slight fatty infiltration. The valves on the right side were normal. The left auricle was normal. The mitral valve was slightly thickened, and full of yellow spots. The aortic cusps were in the same condition. At the apex of the left ventricle there was an opening about 2.5 cm. in diameter which was partly filled with a blood clot. The right coronary artery showed marked arteriosclerosis and some narrowing of the lumen, but no complete closure at any point. The left coronary was in the same condition; the rest of the wall of the left ventricle showed a marked brown atrophy. Old aneurysm at the apex of the heart with perforation and fatal hemorrhage into the pericardium.

Aorta: Marked irregular fibrous thickening of intima with fatty degeneration; necrosis and calcification. Lesion extended far into media.

Kidneys: Marked arteriosclerosis. Many arteriosclerotic scars of moderate size. Rest of kidney tissue was normal.

CASE 3.—M. P., female, aged sixty-three years, American. Patient entered hospital in September, 1921, with a history of shortness of breath, edema of the legs, and swelling of the abdomen of six months' duration. Her past history was irrelevant. The present illness started a year before admission, when the patient began to experience shortness of breath and weakness on exertion, which since, has been increasing in severity. About six months previous to admission the patient suddenly became very weak and breathless, so that she was forced to stop her work. There was no precordial pain and but slight palpitation. Since that time, however, her feet began to swell and subsequently her abdomen. The physical

examination revealed a patient with signs of myocardial insufficiency in that she was orthopneic, markedly dypsneic, and cyanotic. Clinically, the heart was enlarged and the sounds were everywhere faint, regular, and of poor quality. No murmurs and no friction rub was heard. Blood pressure 130/90. There was evidence of passive congestion at both bases; the abdomen was distended and a fluid wave was well marked. The legs showed pitting edema. The patient expired suddenly after the effort of sitting in bed on the second day after admission.

POSTMORTEM DIAGNOSIS BY DR. OPHULS

1. Arteriosclerosis—general—moderate.
2. Arteriosclerosis—local—of coronary arteries with obstruction of the right coronary artery and aneurysm of the left ventricle.
3. Emphysema, senile.
4. Cirrhosis, incipient.

Heart: Specifically the pericardium contained 150 c.c. of pure blood. There was marked bleeding from a ruptured coronary vein over the anterior surface of the septum 5 cm. above the apex of the heart. There were some old, fairly easily broken adhesions at the apex. The heart was very large,—about two and one-half times the normal size. The right auricle and right ventricle were considerably dilated. The right ventricle was somewhat hypertrophied; the muscle averaged 4 mm. The left auricle and left ventricle were definitely dilated. The muscle of the left ventricle was firm, dark brown, and averaged 10 mm. The enlargement of the left ventricle was due to an aneurysmal sac situated at the apex, at the point of the adhesions. The sac measured 6 cm. in diameter and was about 4 cm. deep. The wall of the sac was very thin and fibrous, averaging between 2 and 3 mm. The valves were normal. The right coronary artery showed a marked arterial sclerosis and was obstructed completely, 3 cm. from the point of origin by an old organized thrombus. The left coronary artery was small, and showed marked arterial sclerosis but no obstruction.

Aorta: Marked atheroma.

Kidney: Moderate arterial sclerosis; many small scars in cortex.

NOTE: The right coronary artery in this heart showed evidence of thrombosis, while the left artery was small but showed no obstruction. This is unusual considering the tremendous bulging at the left apical region. It is unfortunate that no x-ray plates were obtained as the contour of the left border was changed by the large aneurysm at the apex.

CASE 4.—J. W., male, aged forty-three years, American. Patient was under observation from 1918 to 1923 in the Stanford wards of the San Francisco hospital, Tuberculosis Department. He suffered from chronic pulmonary tuberculosis with cavitation at the right top and fibrosis with activity at the left apex. Sputum was positive for tuberculosis; blood Wassermann was negative. During the last six months, the patient began to lose weight and strength and was confined to bed. Patient suddenly became comatose, remained in such a state four days and expired. Attention was directed toward the patient's pulmonary condition and disease of the heart was not suspected.

POSTMORTEM DIAGNOSIS BY DR. OPHULS

1. Tuberculosis chronic—lung.
2. Emphysema.
3. Pleurisy.
4. Arteriosclerosis—general.

5. Arteriosclerosis—local—coronaries with scars in the heart muscle; thrombosis left ventricle.
6. Arteriosclerosis of kidneys with scars in kidneys.
7. Aneurysm of heart; septum.

Heart: Specifically—50 c.c. clear fluid contained in the pericardium. Heart was slightly enlarged especially on right side. Right auricle, and right ventricle were dilated and somewhat hypertrophied, the thickness of muscle being 4 mm. Thrombus, cherry-sized, apex left ventricle. Left ventricle was slightly dilated, wall was thin at apex where it measured 3 mm. Membranous septum was slightly thickened and bulged into right ventricle forming a pocket 2 cm. wide and 1 cm. deep. A few yellow spots were noted on the left aortic valve and base of aorta. Right coronary artery was slightly thickened and dilated. Left ventricle, normal vessels, many small scars.

Aorta: A few areas of fatty degeneration of intima.

Kidneys: Arteries slightly thickened; numerous small infarcts in cortex in both kidneys. Embolism right renal artery with infarcts in kidney.

CASE 5.—A. S., aged fifty years, male, Swiss. Patient entered San Francisco hospital (Stanford Ward) in June, 1917 and expired suddenly nine days after admission. The patient had been studied previously in the same ward, at which time the following history was received. Four years ago, the patient contracted a chancre for which no treatment was received. The blood Wassermann was positive. About a month before death he suddenly became weak and unable to work because of shortness of breath. Some days after this, the patient experienced a constant pain over his heart which radiated to the epigastrium, causing vomiting. On entry the patient was orthopneic, cyanotic, and complained of persistent pain over the precordium. Physical examination showed the heart enlarged to the left and downward. A systolic murmur was noted at the mitral area. The aortic area was apparently uninvolved. The pulses were synchronous, and regular in rhythm, but irregular in force. Pupils were irregular and unequal; they reacted to light; knee jerks present. The patient improved somewhat under specific treatment, and was allowed to return to his home. He reentered the hospital in two weeks with the above symptoms aggravated and expired suddenly after seven days observation.

ANATOMICAL DIAGNOSIS BY DR. OPHULS

1. Syphilis of aorta.
2. Syphilis of heart.
3. Syphilitic myocarditis.
4. Aneurysm of heart.
5. Gastritis, acute.

Heart: Specifically—pericardium contained about 50 c.c. of slightly bloody fluid. Milk spot at tip of left ventricle. Heart was about twice normal size. Apex formed by the left ventricle. Right auricle and right ventricle were moderately dilated, and slightly hypertrophied. Muscle was firm about 4 mm. in diameter (ventricular muscle). Left auricle was moderately dilated; endocardium thickened. Left ventricle showed marked dilatation. Heart valves were normal. Both right and left coronaries were normal. Heart muscle on left side was rather flabby, somewhat discolored, and averaged 12 mm. in thickness. Posterior wall of the left ventricle was quite thin, especially behind a small flap of mitral valve. It averaged 7 mm. only, and showed marked bulging at this point.

Aorta: Arch of the aorta showed marked irregular scar formation. Microscopically, tissue taken from this section showed marked round-celled infiltration,

fibrous thickening of the adventitia; marked endarteritis of the vaso vasorum; numerous areas of round-celled infiltration in the muscle; marked irregular fibrous thickening of the intima with fibrous degeneration and necrosis involving the upper layers of the muscle.

Kidneys: Very marked passive congestion and edema; slight arteriosclerosis.

NOTE: In view of the fact that both coronaries were patent and that syphilitic inflammatory changes were noted in both the aorta and heart muscle, it is possible that the aneurysm described is on a localized inflammatory basis in the heart wall and not dependent on arterial disease with thrombosis.

CONCLUSIONS

1. The above small series shows the paramount rôle coronary arterial disease plays in aneurysm of the heart. Here coronary sclerosis is but part of a generalized vascular sclerosis from which the heart muscle has suffered most.

2. The inflammatory changes caused by syphilis do not assume the same importance in aneurysm of the heart as in aneurysm of the aorta.

3. A history of symptoms referable to cardiac infarction is obtained in some cases; in others an exacerbation of symptoms referable to myocardial failure without precordial pain is an outstanding feature.

4. History, physical examination, electrocardiographic and radiographic studies at times fail in the diagnosis of aneurysm of the heart, but the combination of such studies allows one to suspect such a condition with a greater degree of accuracy.

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THE ELIMINATION OF THE EFFECTS OF ALTERNATING CURRENTS ON THE STRING GALVANOMETER

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THE effects of alternating currents in the vicinity of a string galvanometer are frequently so pronounced as to cause the resulting electrocardiograms to be indistinct and distorted. This is brought about by the constant oscillation of the string, synchronously with the alternations of the current in the house line and produced by induction through the patient. This annoyance is most pronounced on damp and rainy days. High voltage lines supplying x-ray machines, elevators, lighting systems, and even telephone lines in close proximity of the electrocardiograph are the chief sources of trouble.

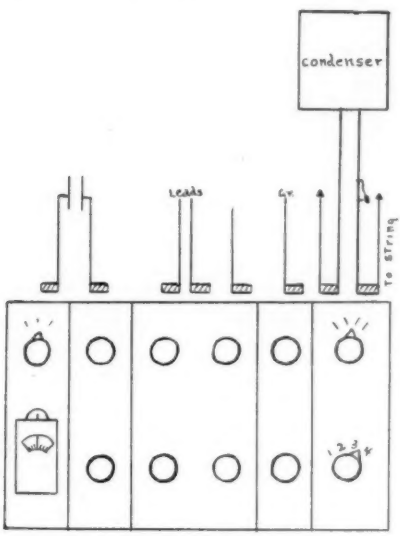
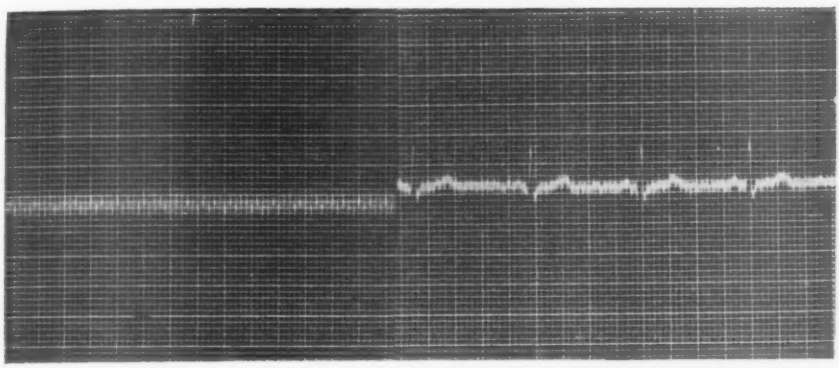


Fig. 1.—Showing the placing of the condenser in the circuit.

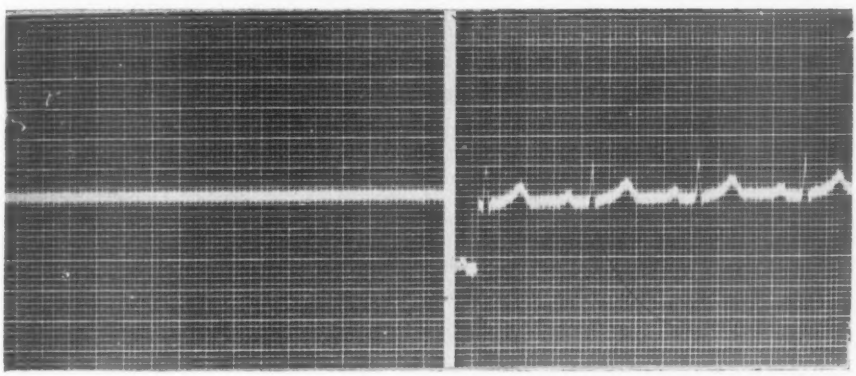
Various means have been devised to obviate these effects, such as screening off the patient, grounding the patient, etc., but these methods are uncertain, cumbersome, and time-consuming. The psychic effect of such paraphernalia upon the subject may be disturbing.

I have found that these extraneous effects may be entirely eliminated by the simple expediency of shunting across the string's circuit a fixed condenser, such as is commonly used in radio receiving sets. The condenser permits the slow frequency electrocardiographic currents to pass through unaltered and filters out the relatively high frequency

alternating currents. It is of some advantage to place a switch in series with the condenser so that this may be cut out at will. The capacity of the condenser necessary will vary between 1 and 4 microfarads, depending upon the conditions encountered.



A



B

Fig. 2.—*A*. Without condenser. Note rapid vibration of string with resultant blurring. *B*. With condenser. String absolutely quiescent giving a sharp and clear shadow.

The accompanying sketch and electrocardiogram are self-explanatory. It can readily be seen how much the electrocardiograms are improved by a completely quiescent string. The deflections are clear cut and elegant.

This accessory is very inexpensive, everywhere obtainable, and easily attached, becoming a permanent part of the equipment. It does not alter the resistance of the string's circuit, and clear cut electrocardiograms result.

Department of Clinical Reports

HEART-BLOCK WITH CONVULSIVE SYNCOPE

Case Report and Pathological Findings in a Patient Unsuccessfully Treated with Barium Chloride

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and
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THE purpose in recording our clinical and postmortem observations upon the following patient is to record our failure so to stimulate a dormant idioventricular pacemaker as to enable it to function and thereby prevent periods of prolonged ventricular asystole. A possible cause of such failure is discussed in this report.

A. G. S., civil engineer, white, aged sixty-three years, was admitted to the hospital November 9, 1926 for treatment of heart failure accompanied by fainting attacks with and without convulsive seizures.

The patient's past history was essentially negative. Approximately three months before admission the patient, upon climbing hills, began to experience dyspnea. The degree of limitation of effort rapidly increased and was soon accompanied by brief attacks of mental confusion. He continued at work, however, until four days before admission, when he lost consciousness while walking on the street. Consciousness was soon regained and he was sent to his home, where his family physician noted that his heart rate was 18, with rhythm regular. Frequent syncopal attacks occurred during the next few days. During these attacks the heart would apparently cease to beat, and if these periods of asystole were prolonged, convulsive seizures occurred. A heart rate above 20 was never observed.

On admission to the hospital the patient's heart rate was 30; his blood pressure 150/44. Breathing of the Cheyne-Stokes' type was present. The ankles were edematous. Numerous moist râles were demonstrable at the bases of both lungs. The liver was enlarged and tender.

The average heart rate during the following thirty-six hours was 28, subsequent to which time it rose to 74. Coincident with this rise the breathing became regular, and within a few days all evidence of heart failure had disappeared. The rate averaged 60 until the seventeenth day, and no periods of asystole were noted. On November 26, however, following a period of mild mental excitement, the rate suddenly fell to 30 and there was a brief period of asystole without complete loss of consciousness. Throughout the next twenty days his heart rate was very unstable, varying from 20 to 100. Several fainting attacks occurred, and some of these were accompanied by muscular twitching. During these attacks the heart apparently ceased to beat. In the following week there was a second period when the heart beat regularly at a rate which varied from 60 to 70, no unpleasant symptoms being present. Subsequent to this, and until the patient's death, frequent fainting attacks were observed. He died on January 30, 1927 in an attack of convulsive syncope.

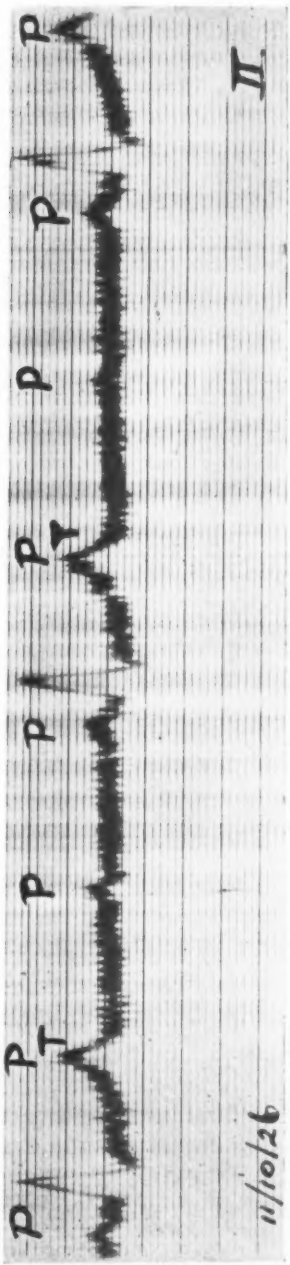

Fig. 1.—Nov. 10, 1926. Lead II. This curve shows an auricular rate of 75, and a ventricular rate of 25. Partial heart-block of this grade was shown on all leads of the electrocardiogram.

Twelve electrocardiograms had been secured during his stay in the hospital. Unfortunately, the equipment of the hospital does not include the wiring of rooms. Hence, galvanometric records could be obtained only when the patient's condition warranted his being taken to the heart station. The record on the day following admission shows the presence of partial heart-block, the mechanism being 3:1 (Fig. 1). Subsequently mechanisms of 1:1, 2:1 and 3:1 were shown. The patient

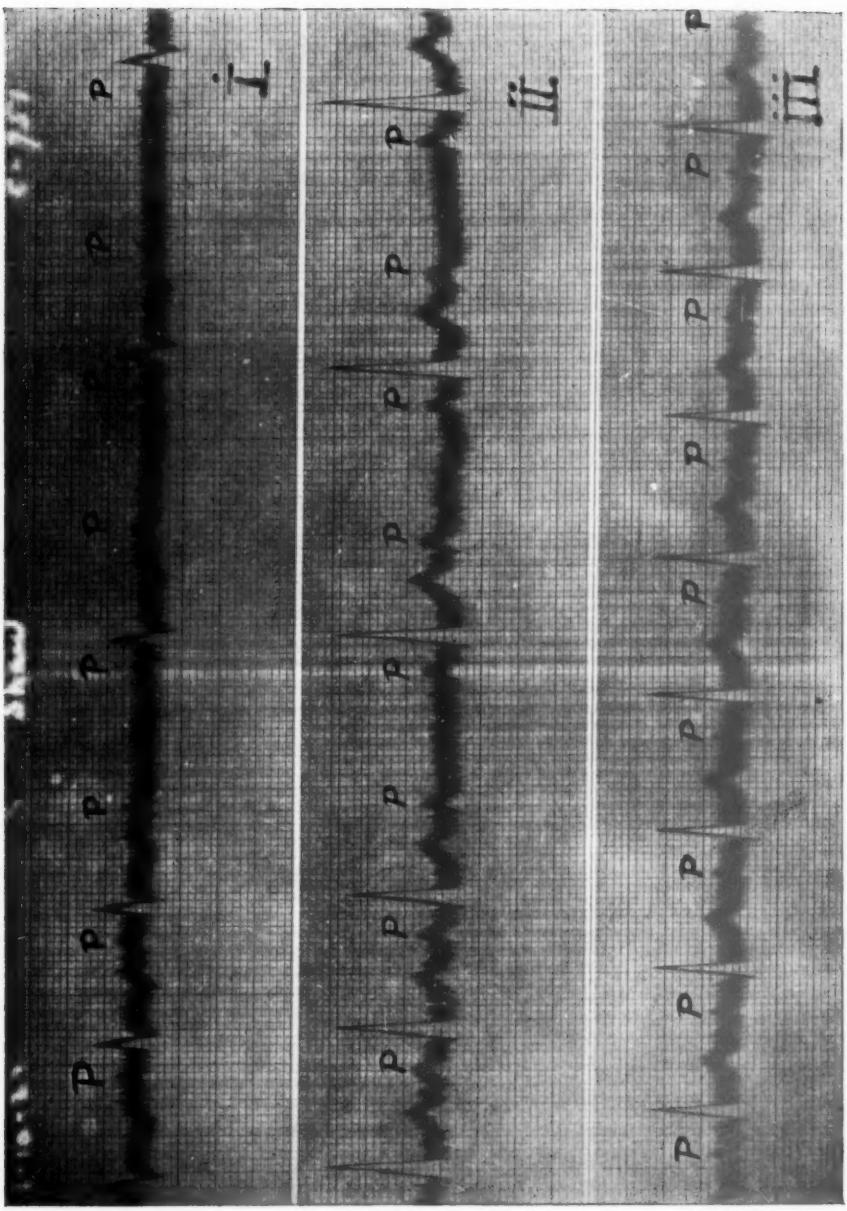

Fig. 2.—Jan. 10, 1927. In this figure are shown Leads I, II, and III. In Leads I and II the first two cycles show a 1:1 mechanism; the following cycles, 2:1. Throughout all cycles of Lead III a 1:1 mechanism is recorded.

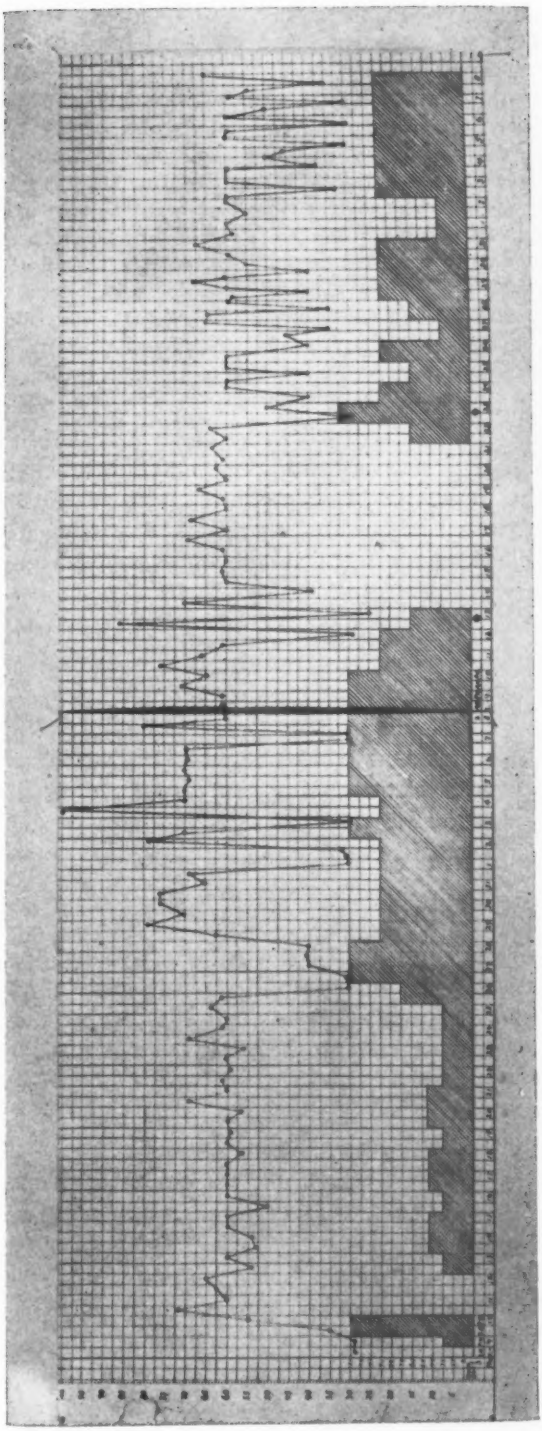

Fig. 3.—Solid line: highest and lowest heart rate as recorded on a given day. Shaded areas: dosage of barium chloride as expressed in milligrams. The initial dose was 30 mg. On the following day 120 mg. were given.

left the hospital on January 10, 1927. The electrocardiogram of this date (Fig. 2) shows a 1:1 mechanism alternating with 2:1. Some degree of deformity of the ventricular complex was observed on all the curves. The longest A-V interval was 0.24 second. No records could be obtained during periods of ventricular asystole, nor was complete dissociation ever demonstrated.

The laboratory reports, including blood Wassermann, were essentially negative.

The x-ray film taken November 18, 1926 is analyzed by Dr. John F. McCullough as follows: Patient was examined in sitting posture as he was too ill to stand. The film was placed in front of his chest with a tube target distance of seven feet. The cardiovascular shadow showed a slight enlargement of the heart to the left. Demarcation of the different bows of the cardiac outline is indistinct. The measurements, as nearly as can be determined, are as follows: broadest diameter of the aorta 7 cm.; longest diameter of the heart 18.5 cm.; from the midline to the right border of the heart 3.7 cm.; from the midline to the left border limit 13.5 cm. There was no evidence of gross lung abnormality.

DISCUSSION

The graph (Fig. 3) records the highest and lowest heart rates observed on given days and also the amount of barium chloride administered during the patient's stay in the hospital. Subsequently 1320 mg. of barium chloride were given. Epinephrin was given subcutaneously or intramuscularly during periods when fainting attacks were frequent, and the patient was fully atropinized for a considerable period of time. Separate consideration of the apparent indication for the use of these drugs and of the patient's response to them follows.

(a) *Barium Chloride.*—This drug was studied by Rothberger and Winterberg[1] and their report, published in 1911, showed that barium and calcium are capable of increasing ventricular irritability. This is evidenced by the development of numerous ectopic ventricular contractions or ventricular tachycardia. Two years later Van Egmond[2] showed that the same effect could be obtained even when complete heart-block was experimentally produced.

Based upon this knowledge previously gained through experiments on animals and upon the clinical results which they had obtained in three cases of Adams-Stokes' disease, Cohn and Levine[3] have recently recommended that barium chloride be given a trial in cases of heart-block clinically associated with syncopal or epileptiform attacks. These authors summarize their observations as follows: "The customary therapeutic procedures including epinephrin did not prevent the recurrence of attacks, whereas barium chloride given by mouth, in each instance, promptly proved successful in rendering patients free from attacks."

Following publication of this report, Hermann and Ashman[4] obtained what they term spectacular therapeutic results from the administration of barium chloride in the treatment of two cases of heart-block with and without convulsive syncope. These authors used heavy dosage of this drug during long periods of time. In one patient, heart-block was complete; in the other, block was partial. It appears

to us that only in the first instance was the result "spectacular." In neither case was there apparent detrimental effect. One patient received a total of 10.98 grams in sixty-seven days, subsequent to which time he took 50 mg. daily; another received a total of 840 mg. during eight and a half days. The first was given an initial dose of 1.3 grams; no ill effect resulted other than the production of nausea, vomiting, and slight diarrhea.

Levine[5] published a second communication stating that he had recently received word from two physicians, who had found barium chloride effective in preventing Adams-Stokes' seizures. In both instances the patients had experienced repeated attacks of syncope, which were promptly controlled by the administration of the drug.

It has thus been shown that barium chloride is capable of stimulating the normal ventricular musculature of animals, this effect being evidenced by the production of ventricular ectopic beats. It has also been proved that in the human subject the administration of barium chloride may abolish fainting attacks when associated with complete heart-block. In complete heart-block, ventricular contraction occurs as a result of an active intrinsic mechanism. In our case of block, no evidence of the presence of an idioventricular rhythm was ever shown. Obviously, the lower pacemaker was refractory to physiological stimulation; it would probably be equally so to that of drugs. Nevertheless barium chloride was given, the patient receiving a total of 5 gm. over a period of about three months, during which there were observed neither favorable nor unfavorable effects. Ectopic ventricular contractions did not appear. The attacks continued with increasing frequency, and in one of these the patient died. We believe that the extensive lesion involving the junctional tissues, subsequently demonstrated and about to be described, may explain our failure to influence the paroxysms.

(b) *Epinephrin.*—Levine and Matton[6] discussed the value of adrenalin when specifically directed to the attacks of syncope which occur in the course of heart-block. They wrote that after an injection of adrenalin a patient usually remains free of fainting attacks for several hours, but as the effect of the adrenalin wears off, the attacks return. If the patient is in syncope at the time of injection, no effect can be obtained because the circulation is then at a standstill. Under such conditions, these authors advised intracardiac injections, and support their recommendation by the report of a case of Adams-Stokes' disease in which occurred attacks of syncope from several seconds to about five minutes in length. "During the very long attacks, adrenalin chloride was injected directly into the heart, and was followed by a prompt recovery."

During the two months that our patient remained in the hospital a hypodermic syringe charged with 0.5 c.c. of epinephrin solution was

kept in his room. He was never alone, and the attendants were instructed as to the technic of intracardiac administration. During none of the patient's attacks was it possible to secure cooperation to the extent of giving the intracardiac injection. This is regrettable in the the case of his final period of asystole. Had such injections been given during previous syncopal attacks, we fear that we might have been tempted to draw wrong conclusions therefrom. Although we knew that the effect of epinephrin lasts but a short time and that the recurrence of attacks of syncope are, therefore, not likely to be prevented, nevertheless we gave epinephrin subcutaneously and intramuscularly in frequently repeated doses during the periods of relatively high degree of block. We were not able to decide whether such administration had any influence upon the course of the case.

(e) *Atropine.*—Cohn and Levine[3] administered atropine to each of the three patients previously discussed. These authors noted that in one case the drug was not only without beneficial effect, but that on the contrary, its use was followed by aggravation of the patient's bad condition. In their other two cases, administration of the drug was apparently useless. In the first patient of Hermann and Ashman,[4] the administration of atropine was followed by a long series of frequent and severe syncopal attacks. The second patient was given a short course of atropine without effect. During the course of the case here reported, the administration of atropine apparently failed to influence the degree of block or the frequency of syncopal attacks.

Pathological Description of the Heart.—The heart was removed from the body about one hour after death. Unfortunately, permission could not be obtained for complete prosection of the body, but only for removal of the heart. The body showed large deposits of fat everywhere, especially in the subcutaneous tissues and in the omentum. The liver extended about 2 cm. below the costal margin, but did not appear to be of the type due to chronic passive congestion. The kidneys on gross examination in situ showed no abnormalities.

The heart was immediately examined in the gross and sections were taken from the various portions and fixed at once in Zenker's fluid. Serial sections were taken through the atrioventricular node and various portions of the conducting bundle. Three blocks were taken from the wall of the right auricle, one from that wall just at the attachment of the tricuspid valve leaflet, one from the right ventricular wall, and four from the course of the bundle-branch in the left ventricular wall. These blocks were all taken at right angles to the course of the bundle and so sectioned that cross sections of the different parts were obtained. These were then stained with hematoxylin and eosin, eosin and methylene blue, and phosphotungstic acid.

After having been opened and the blood clot removed, the heart weighed 625 grams. Its tone throughout was quite good although the right ventricle was slightly dilated. There was a very large amount of subepicardial fat, especially over the right ventricle where the thickness was 1.2 cm. The wall of the left ventricle was hypertrophied, measuring 1.6 to 2.2 cm. in thickness, and the muscle had the grayish appearance of slight fibrosis. Both coronary arteries were markedly sclerosed, especially the anterior, but there was no evidence of infarction of the

muscle. The valve leaflets were normal, except for some fine atheromatous patches on the mitral leaflets. The root of the aorta showed some fine, yellow, atheromatous patches but none of the puckering caused by a medial fibrosis.

The foramen ovale was closed and just below and anterior to it, the beginning of the atrioventricular node could easily be seen. This area seemed to be slightly raised and to have a yellow, fatty appearance through the endocardium. The course of the bundle could be readily followed by this appearance, and about half way between its beginning and the auriculoventricular junction it was imbedded in firm, fibrous tissue of a cord-like feeling. Immediately above the attachment of the tricuspid valve there were two yellow, fibrous patches beneath the endocardium. These patches each measured 0.5 x 0.1 cm. on the surface and lay parallel to the base of the valve; they were about 0.2 cm. apart so that the atrioventricular

Fig. 4.—Low power magnification of the fibrotic patch noted in the wall of the right auricle. The conducting fibers are compressed by the dense fibrous tissue and are in various stages of degeneration.

bundle ran between them and was pressed upon from either side. When sectioned, these areas were found to consist of dense fibrous tissue, and one of the microscopic preparations showed very plainly the relationship between these and the bundle. The course of the right bundle-branch down the ventricular wall could not be followed by its gross appearance, while that of the left branch could be easily seen. It was plainly visible where it emerged from beneath the aortic valve leaflet and stood out beneath the endocardium as a slightly raised, grayish band, 0.4 cm. in width. On section through this band the fibers immediately beneath the endocardium were noted to retract more than the cardiac fibers proper. The microscopic preparations proved them to be Purkinje fibers. This band, as it progressed down the ventricular wall became less distinct and was finally lost among the pectinate muscles. The entire endocardium in this region had a pale, gray, fibrosed appearance.

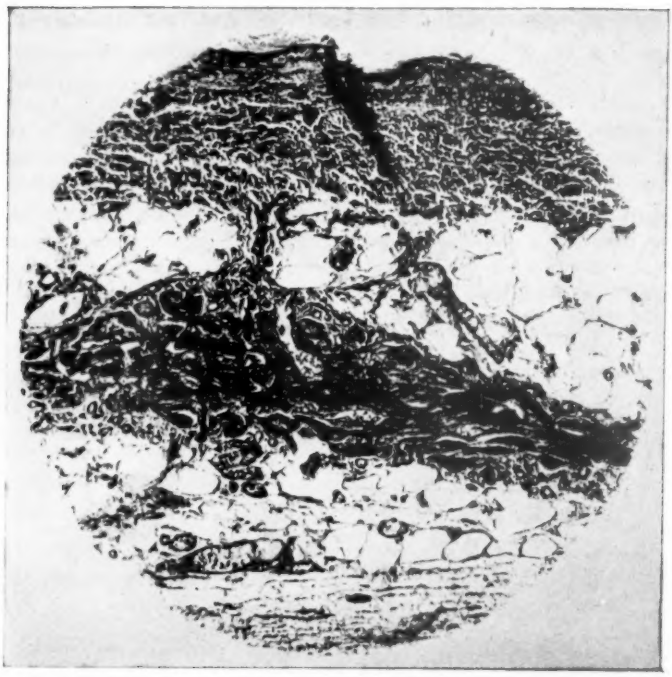

Fig. 5.—Higher power of the bundle of His just below the A-V node, showing fatty infiltration.

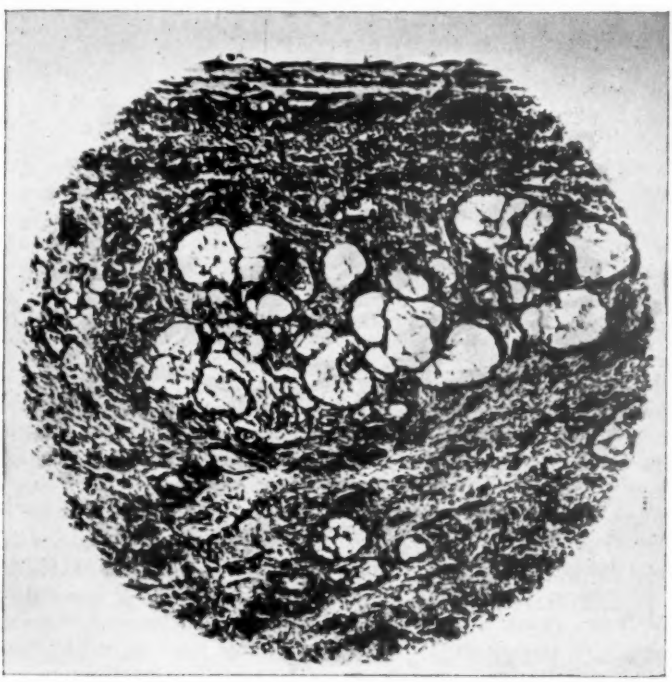

Fig. 6.—High power reproduction of a portion of the left bundle-branch showing the markedly degenerated Purkinje fibers, only the sarcolemma remaining in some.

Microscopical Findings.—The outstanding features of the microscopical findings were those encountered in the course of the conducting bundle. In the sclerotic patch noted on the wall of the right auricle just at the base of the tricuspid valve was found a very dense, subendocardial fibrosis, and the main part of the right bundle-branch was enclosed in this process. This is well illustrated in Fig 4, which is a low power reproduction of that area. The bundles themselves were broken up and their individual fibers were separated and compressed by the ingrowth of this fibrous tissue. In this reaction, however, there was no infiltration of lymphocytes as has been noted by various authors[7, 8] in such lesions in syphilitic hearts. Also there was neither sclerosis of the adjacent vessels nor hyperplasia of their endothelium. A few of the conducting fibers appeared normal, but the greater number showed some stage of degeneration. These were smaller than usual, with

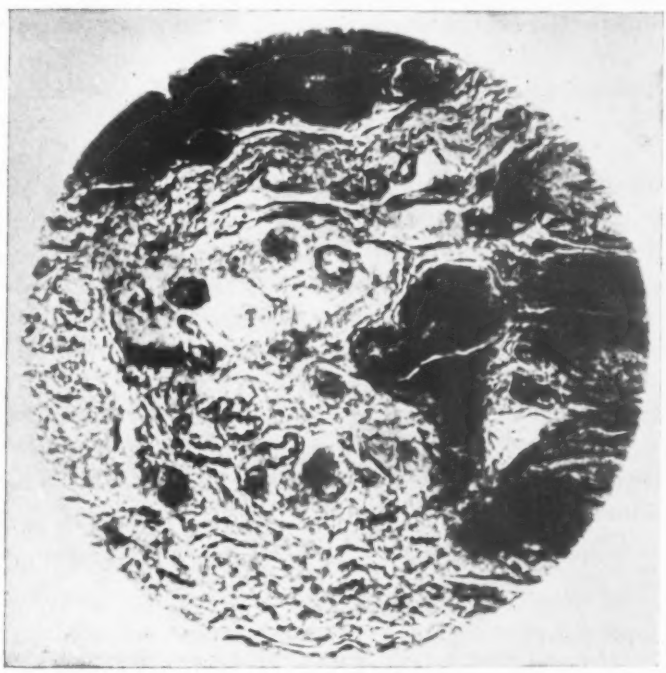

Fig. 7.—High power reproduction of the left bundle-branch showing endotheliocytes phagocyting the degenerating Purkinje fibers.

their myofibrils deeply stained and close together, and in only a few was a nucleus visible. Others showed only a sarcolemma with a few scattered myofibrils just beneath it. In many, the sarcolemma had divided the individual fibers into two or more separate parts: a finding which Van der Stricht and Todd[8] believe indicates degeneration. On the opposite side of this section (left auricular side) could be seen a few fibers of the left bundle-branch with a normal appearance.

Sections of the auricular wall immediately above this area showed the conducting bundles to be more intact, and the individual fibers to be practically normal in appearance. About the bundles of fibers, however, there was a quite marked fatty infiltration with a number of lymphocytes. Smaller vessels were numerous and some of these showed a slight hyperplasia of their endothelium and a perivascular infiltration of lymphocytes. Other sections taken above this area showed a similar picture.

Sections of the left bundle-branch, taken from the ventricular wall just beneath the aortic valve leaflet, (Fig. 5) showed the Purkinje fibers well spread out beneath the endocardium. The fibers were separated by a moderate amount of dense, fibrous tissue and showed varying degrees of degeneration. In some instances only a few myofibrils remained about the periphery, while in others (Fig. 6) there was left only the sarcolemma and the fibrillar network of the sarcoplasm. In a few fibers in which the myofibrils were markedly degenerated, small and granular, there were a number of endothelial cells which were engaged in phagocyting the cellular remains (Fig. 7). While the fibrosis was mostly limited to the subendocardial area in the region of the conducting bundle, there was some slight interstitial fibrosis extending throughout the ventricular myocardium.

SUMMARY

A case of partial heart-block is reported in the course of which there occurred frequent attacks of syncope with convulsive seizures (Adams-Stokes' syndrome). During the period of observation barium chloride, epinephrin and atropine were administered,—all without appreciable effect. The patient died during an attack of ventricular asystole. Postmortem examination showed a lesion involving junctional tissues and consisting of a fatty and lymphocytic infiltration of the atrioventricular node and the first part of the bundle of His together with a fibrotic process involving both left and right bundle-branches. The bundle fibers showed degeneration. That this degeneration was active, was evidenced by the finding of endotheliocytes which were phagocyting the degenerating Purkinje fibers.

We suggest that our failure to establish an idioventricular rhythm might have been due to the presence of extensive destruction of junctional tissues in a patient in whom the lower pacemaker had never been dominant.

The authors are indebted to Dr. S. R. Haythorn for the photomicrographs.

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SIGNS OF AORTIC INSUFFICIENCY IN ABSENCE OF AORTIC LESION*

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THE diagnosis of aortic insufficiency is usually based upon the presence of a high-pitched, blowing diastolic murmur together with evidence of cardiac enlargement and certain peripheral signs such as throbbing arteries, water-hammer pulse, capillary pulsations, high pulse pressure, and pistol-shot sound or Duroziez' murmur over the femoral arteries. The murmur may be due to causes other than aortic insufficiency, and no one of the peripheral signs is pathognomonic, but the presence of the typical murmur together with the peripheral signs is usually considered adequate basis on which to make a definite diagnosis of aortic insufficiency. The following case is reported because practically all of the signs of aortic insufficiency appeared while the patient was under observation, but at postmortem examination no disease of the aorta or of the aortic valves could be demonstrated.

An eighteen-year-old boy was admitted to the 1st Medical Division of the New York Hospital on December 28, 1925, because of severe cardiac decompensation. He gave no history of rheumatism, chorea or tonsillitis, and was said to have been robust until 1916 when he collapsed following a foot race. After that he was never strong. He was in the hospital three times in 1920 and 1921, each time with a diagnosis of chronic cardiac valvular disease, mitral insufficiency and stenosis, but except for these periods he had been fairly well. At the time of admission physical examination showed a poorly developed and poorly nourished boy, appearing acutely and chronically ill. He was dyspneic and orthopneic; face, ears and fingertips were cyanotic; legs and back were edematous, and there was fluid in abdomen and in right chest. Veins of the neck were engorged and showed marked systolic pulsations, and the hard pulsating liver extended 8 cm. below the costal margin in the nipple line. The heart was enlarged to left and to right, with quick apex impulse visible in fourth, fifth and sixth spaces as far out as the anterior axillary line. Rate was 144; rhythm regular. Pressure on vagus caused marked slowing of the rate. The first sound at the apex was sharp and accentuated, preceded by a crescendo murmur and accompanied by a loud blowing systolic murmur. At the pulmonic area the second sound was accentuated and accompanied by a shock. Blood pressure was 142/69 mm. of Hg. A diagnosis of auricular flutter was made and was confirmed by electrocardiogram.

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Under the influence of digitalis the flutter changed to fibrillation and the general condition slowly improved. The following notes, taken from the chart, describe the physical signs:

December 31. Patient is much better today. There is an accentuated first sound accompanied by a blowing systolic murmur, a tapping second sound, and a short diastolic rumble. At times the rumble leads up to the first sound, but usually there is a short pause between rumble and sound. At the base second pulmonic sound is accentuated.

January 3. Digitalis has produced a noticeable diuresis. There is still fluid in the abdomen and in the right chest. Patient feels much better.

January 8. The question of aortic insufficiency has been raised. There is a faint diastolic murmur heard at the left of the sternum but this is not constant. There is a capillary pulse; arterial pulse is not definitely collapsing; no pistol-shot sound or Duroziez' murmur.

January 14. The heart is fibrillating slowly. Forceful wavy impulse is seen over most of the precordium, most marked in the sixth space at the anterior axillary line. By percussion cardiac dulness measures in the second space 2.5 cm. to right and 1.5 cm. to left, in the third space 2.5 and 4 cm., in the fourth space 5.5 and 8 cm., in the fifth space 12 cm. to the left and in the sixth space 14 cm. to the left. First sound at apex is very sharp and second pulmonic is accentuated. There are systolic and diastolic murmurs at apex and also a faint, high, diastolic murmur over aortic area and at left of sternum. Pulse is collapsing. Over femoral arteries there is pistol-shot sound, and in addition to systolic murmur caused by pressure of stethoscope a short diastolic murmur. Liver dulness extends to fourth space anteriorly; edge is palpable 5 to 6 cm. below costal margin. Liver does not pulsate. There does not appear to be free fluid in abdomen. Resonance is impaired over right chest posteriorly below level of ninth dorsal vertebra; voice and breath sounds are not changed. There is no edema of legs or back. Patient is up and about ward and feels well.

On January 18 the patient was discharged with the diagnosis of mitral stenosis and insufficiency, aortic insufficiency, and auricular flutter changed to fibrillation. Following discharge he continued to take 20 minims of the tincture of digitalis each night and he remained comfortable until February 9 when he became short of breath and began to vomit persistently. He was readmitted to the hospital on February 13 and remained in the ward until his death on March 18.

At the time of admission dyspnea, orthopnea and cyanosis were present; liver and jugular veins pulsated; there were signs of fluid in abdomen and in right chest. The heart was fibrillating rapidly; sounds and murmurs had not changed since the time of discharge. The pulse was not typically collapsing; diastolic murmur and tapping sound were heard over the femoral arteries. The blood pressure was

estimated at 132/40 mm. of Hg. The heart rate became slow under the influence of digitalis. The heart signs then remained unchanged except that later the pulse was again described as collapsing. The rate remained slow.

On February 18 the temperature was elevated and that night there was sudden excruciating pain in the left axilla. Later signs of consolidation were present over the left lower lobe. On March 4 there was a chill followed by cough and blood stained sputum and signs of consolidation over the right lower lobe. On March 7 the blood culture was reported to show a pure growth of pneumococcus, group IV. The condition became progressively worse and on March 17 the patient lapsed into coma with widely dilated pupils, deviation of the eyes to the left, and spasmodic twitchings of the left side of the body. Turbid greenish yellow spinal fluid was withdrawn. The globulin was markedly increased and there were 600 cells per c.mm.

The patient died early on March 18 and autopsy was performed by Dr. Semsroth four and a half hours later. The postmortem findings were of particular interest in that they failed to confirm the clinical diagnosis of aortic insufficiency. The pericardial cavity was obliterated by dense and fine adhesions. The heart was enlarged and with the pericardium weighed 675 grams. The muscle was chocolate colored and on microscopic examination showed patchy areas of dense infiltration with poly- and mononuclear cells. The mitral valve was the seat of extensive calcific nodules. Some of these were rough and red; others were covered by smooth endocardium. One soft, friable vegetation was snipped off, washed, and on culture this yielded a pure growth of group IV pneumococcus. The aortic, pulmonary, and tricuspid valves and the aorta appeared normal in all respects. Additional findings were the presence of pleural adhesions; of consolidation of the right upper, right lower, left lower and part of the left upper lobes; left interlobar empyema; infarcts of kidneys and spleen; pyelitis; suppurative hepatitis, nephritis, meningitis and encephalitis. Microscopic examination of the consolidated lung showed brown induration; culture of interlobar pus yielded pneumococcus.

COMMENT

This case has been reported because the clinical signs of aortic insufficiency were not confirmed by the postmortem examination. The lesions actually found were mitral stenosis and insufficiency and adherent pericardium. During life there had been no signs directing attention to the possibility of an adherent pericardium, and because of the arterial signs the murmur had not been interpreted as a Graham Steele murmur. Another interesting feature of this case was the appearance of acute pneumococcus endocarditis in a patient with old mitral stenosis and auricular fibrillation.

ACUTE STAPHYLOCOCCUS AUREUS ENDOCARDITIS

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A RATHER unusual case came under my observation recently which merits being put on record.

On February 11, 1927, I was asked to see a young woman who, the attending physician thought, had epidemic cerebrospinal meningitis. The patient, a well-built, unmarried girl, seventeen years old, had suddenly gone into convulsive seizures that morning. She had never been ill before. She had passed through the common exanthemata with no serious difficulties. She had never had rheumatic fever or any of the associated rheumatic maladies. She was unusually strong in build and endurance. Three days before she was taken ill she had attended a dance.

The parents, brothers and sisters were all healthy. They came of German peasant stock.

The history obtained from the mother was that during the early part of the week (four to five days previously) she was in her usual good health except for a slight cold. February 9 she complained of headache and backache but was up and about as usual. She came home on the afternoon of February 10 apparently in her usual good health. She remarked that she was tired and thought she would go to bed early. About 6 A.M. on February 11 she was taken with a convulsion. From that time on she passed from one convulsion into another, never becoming conscious between convulsions. A physician was called about noon who noted rigidity of the entire body including the neck. He found positive Babinski, Gordon and Oppenheim reflexes, ankle clonus and increased knee jerks. His tentative diagnosis was meningitis.

When I saw her about 2 P.M., the following conditions were present: A strong well-built young woman was lying in bed frequently stiffening all the muscles and throwing arms and legs about in a purposeless manner. She did not respond to question. The pupils were unequal, reacted sluggishly to light. The left was larger than the right and there was left conjugate deviation. The lids were half closed. The respirations were rapid and shallow, alternating with periods of fairly normal respiration. No paralyses or weakness of any group of muscles could be made out. The neck muscles were not stiff. There was no Kernig's sign. In the convulsive seizures the hands and feet assumed the carpopedal spasm position of tetany. The pulse was rapid and of small volume, from 112 to 130 per minute, regular in force and rhythm.

The axillary temperature was 106.2° F. Nothing abnormal could be found in the lungs, heart, or abdomen.

It seemed that the most probable diagnosis was a fulminating encephalitis. I had seen somewhat similar cases of this disease during the past few years. A lumbar puncture was attempted, but because of the impossibility of holding her in position the puncture was unsuccessful. Only pure blood was obtained. She was removed to hospital where a spinal puncture was done. The fluid was clear and contained 20 cells to the cubic millimeter. No globulin was present.

Within two hours of entrance to hospital the temperature was 107.5° F. and she was in deep coma with rapid respiration and thready, rapid pulse. She died at midnight, thirty hours from the onset of the first convulsion with an antemortem temperature of 108.6° F.

The diagnosis was acute epidemic encephalitis. Fortunately an autopsy was obtained. Dr. Wm. Thalhimer performed the autopsy and the bacteriological studies were done at Columbia Hospital.

The body was that of a well-nourished white girl. Scattered over the skin were a number of discrete, small purplish spots from 1-3 mm. in diameter, some of which had pale centers.

Over the surface of the brain were numerous petechial hemorrhages and the vessels of the sulci were engorged. The lungs showed numerous petechial hemorrhages throughout as well as over the pleural surfaces. The pericardial sac contained about 100 c.c. of clear yellow fluid. The heart was of normal size and scattered over the surface were numerous petechial hemorrhages with pale centers. On opening the heart similar hemorrhages were seen through the endocardium and seen also in cut section of the muscle. Both the mitral and tricuspid valve leaflets were thickened producing considerable stenosis of both orifices, especially the mitral. There was slight thickening of both the pulmonary and aortic cusps. Superimposed upon the thickened mitral valve was a dark-colored, only slightly raised, recent, small, warty vegetation extending along the valve for about 1 cm., and extending down upon the chordae tendinae of the anterior leaflet. The kidneys had a mottled appearance with great numbers of petechial hemorrhages over the surfaces as well as several small recent infarcts. Cut section showed cloudy swelling with congestion and petechiae. The spleen was only slightly enlarged, was softer and darker than normal, and contained several small grayish infarcts. The liver was the seat of cloudy swelling. There were numerous petechiae over the surface as well as over the whole peritoneal surface. The pelvic organs were normal. From direct smears of the vegetation on the mitral valve Gram-positive cocci were found. Cultures made from this spot from the heart's blood and spleen all showed pure growth of Staphylococcus aureus.

Microscopic sections of the heart showed cloudy swelling of the fibers with marked fracture. In almost every section are several areas composed of polynuclear leucocytes and masses of cocci. Many bacterial emboli are seen in the small vessels. Sections stained with methyl-green-pyronin showed a few characteristic Aschoff bodies staining typically. These have the appearance of being of long standing and of undergoing some fibrosis. The mitral valve shows a very marked fibrosis. Upon the surface and for a short way into the depth of the valve are masses of cocci.

COMMENT

The results of the autopsy were a complete surprise. This girl was not known to have had any disease which could have damaged her valves and her whole illness lasted less than two days. Careful search failed to reveal the source of the fatal infection. The usual organism was not found but an organism which in itself is not a common cause of malignant endocarditis. The widespread distribution of bacteria was a striking feature. Petechial hemorrhages which show pale centers are said by Libman to be characteristic of infection with the Streptococcus viridans. Here was an infection with the Staphylococcus aureus producing a pathological picture similar to that produced by the Streptococcus viridans.

The potential danger of damaged valves is illustrated in this case. The septicemia unquestionably had its source in the bacteria from the mitral vegetations. Whence the bacteria came on the valve is a question which cannot be answered.

Department of Reviews and Abstracts

Selected Abstracts

Weiss, Edward: Congenital Ventricular Septal Defect in a Man, Aged Seventy-Nine. Arch. Int. Med., 1927, xxxix, 705.

The case reported is unique in the peculiar location and large size of a congenital ventricular septal defect unassociated with other anomalies. The age of the patient and the absence of cardiac symptoms other than a terminal cyanosis are additional features of interest. The patient was admitted to the hospital and died, at which time an autopsy was performed.

Eyster, J. A. E., Meek, Walter J. and Hodges, F. J.: Cardiac Changes Subsequent to Experimental Aortic Lesions. Arch. Int. Med., 1927, xxxix, 536.

In the present series of experiments the progress and extent of cardiac enlargement following experimental stenosis and regurgitation in dogs were studied by the determination of areas of roentgen-ray silhouette of the heart taken at a distance of one meter from target to film and correcting for distortion. The first series of experiments comprised 19 dogs in which aortic stenosis was produced by a constricting band placed about the aorta immediately above the valve. Attempts were made to produce stenosis in 28 animals. Eighteen animals recovered completely from the immediate effects of the operation and were observed for periods varying from 28 to 148 days. In 15 dogs experimental aortic regurgitation was produced by the introduction of a valvulotone through the right carotid artery. In all but two animals one valve leaflet alone was cut. In two, 2 valve leaflets were bisected. Roentgen-ray and electrocardiographical observations were made, as in the stenosis series.

Experimental aortic stenosis and insufficiency in dogs is usually associated with a gradually developing cardiac hypertrophy. This hypertrophy is preceded by a stage of initial dilatation usually passing off in part or completely within a few days. There are no electrocardiographical changes characteristic of the early dilatation or hypertrophy subsequent to aortic lesions. Even an extreme degree of dilatation in the normal heart fails to cause significant changes in the electrocardiogram.

The histological changes following aortic regurgitation are those characteristic of simple hypertrophy without evidence of degenerative processes in the cardiac muscle.

Bacon, Charles M. and Apfelbach, Carl W.: Primary Sclerosis of the Pulmonary Artery and Its Branches. Arch. Path. and Lab. Med., 1927, iii, 801.

Primary or genuine sclerosis of the pulmonary artery and Ayerza's disease are two clinical entities which have been studied with increasing frequency during the last twenty-five years. Even though diminution of the pulmonary artery bed by sclerosis of the pulmonary artery and its branches is the essential morbid alteration ascribed to both of these diseases, the clinical manifestations, as described by their exponents, are in many respects dissimilar. Most authors describe syphilitic arteritis of the pulmonary artery in Ayerza's disease, whereas in the other disease syphilis generally has been excluded and another single common etiological factor has not been found.

The clinical and anatomical characteristics of primary sclerosis of the pulmonary artery are described, and a report is made of one case that the authors believe is typical of this disease.

Even though primary sclerosis of the pulmonary arteries is a rare disease, its anatomical and clinical manifestations are so characteristic that it should be recognized during life, if it is borne in mind when search is being made for the cause of enlargement of the right side of the heart.

Ayerza's disease has not been defined clinically and anatomically as characteristically as primary sclerosis of the pulmonary arteries. Some of the cases reported as Ayerza's disease resemble the latter disease, but others are obscured by extensive alterations in the lungs and by associated cardiac disease.

Drury, A. N. and Jones, N. W.: Observations upon the Rate at Which Edema Forms When the Veins of the Human Limb Are Congested. Heart, 1927, xiv, 55.

In this paper the results are reported of the investigation into the rate at which edema forms in the leg of the normal human subject when the venous pressure is increased locally by means of a pressure cuff applied to the thigh. The increase in leg volume has been measured by means of a specially devised plethysmograph which imposes no pressure upon the limb, which is free from air leaks and can be adjusted quickly upon the limb. The rate at which edema forms has been estimated by measuring the increase in volume from the tenth to the thirtieth minute after cuff pressure has been applied to the veins. The increase during this period as is shown is due solely to edema.

The rate at which edema forms increases as venous pressure is raised. It is increased by rise of external temperature. Transudation rate gradually declines as edema fluid collects in the limb.

Distinct measurements of the transudation rate are comparable only

if like pressures and temperatures are employed and only if the fluids of the tissue spaces are normal in their initial quantities, or, if increased, equal in their initial amounts in the cases compared.

The measured rate remains constant within narrow limits from day to day in any given subject leading a sedentary life. Considerable variation is found when different subjects, all leading sedentary lives are compared.

Short strenuous running exercises and long continued walking change the transudation rate, and the pre-exercise rate is not restored until about twenty-four hours later.

Palpable edema occurs when the amount of collected tissue fluid increases the limb volume 8 per cent.

Harris, Kenneth E. and Marvin, H. M.: A Note on the Temperature of Venous Blood and Its Use in Estimating Rate of Blood Flow to the Hand. Heart, 1927, xiv, 49.

The authors have devised a method for measuring the temperature of the venous blood in situ by means of a thermoelectric junction made from a hypodermic needle. This is so arranged that the needle may be inserted directly into a superficial vein on the dorsum of the hand. They have studied the effect of immersing the hand in a water-bath, the temperature of which lies between 36° and 32° C.

The temperature of the venous blood, when the hand is at rest, the room temperature being between 20.8° and 24.4° C., assumes a level between 34.3° and 35.8° C. Using a water-bath between 26° and 32° C., the average difference between the temperatures of the bath and venous blood in the hand is 1.84° C. after fifteen minutes and 1.31° C. after thirty minutes immersion.

Reid, William D.: Paired Auricular Extrasystoles Simulating Interpolated Extrasystoles of Supraventricular Origin. Arch. Int. Med., 1927, xxxix, 596.

In an electrocardiogram obtained recently from a patient sixty-four years of age, diagnosed as auricular fibrillation, there appear extrasystoles of an unusual type. In an attempt to analyze the nature of these extrasystoles, the author points out the difficulty in differentiating between a true interpolation and pairing of auricular extrasystoles.

Andrus, E. Cowles and Martin, Louis E.: The Action of the Sympathetic upon the Excitatory Process in the Mammalian Heart. Jour. Exper. Med., 1927, xlv, 1017.

The present study was undertaken in an attempt to examine certain phases of the action of the sympathetic nerves on the heart of cats and dogs. The authors studied the effect of sympathetic stimuli on intra-

auricular conduction by injections of adrenalin solution. They also studied the paralyzing effect of ergotomine on the sympathetic endings.

When the action of the parasympathetic nerves has been excluded by means of atropine, it is possible to demonstrate that the excitatory process in the heart is affected, to a considerable degree, by the control of the sympathetic nerves. From all phases of excitation and conduction in the mammalian heart with the exception of intraauricular conduction, the action of the vagus and sympathetic are opposed. Here the vagus is without effect unless the rate of transmission is abnormally slow. Stimulation of the sympathetic nerves, on the other hand, invariably causes a conspicuous rise in the transmission rate. It is, therefore, apparent, upon closer analysis, that the effects of the vagus and sympathetic nerves upon intraauricular conduction are in no sense synergistic.

Under normal conditions there exists a delicate balance of such a nature that stimulation of one system involves inhibition of the other. It is, however, significant that following paralysis of both sympathetic and parasympathetic nerves, the normal rhythm is maintained spontaneously at a more or less constant rate.

Blumgart, Herrmann L., and Weiss, Soma: Studies on the Velocity of Blood Flow: II. The Velocity of Blood Flow in Normal Resting Individuals, and a Critique of the Method Used. Jour. Clin. Inves., 1927, iv, 15.

The chief precautions observed in estimating the velocity of blood flow by the radium active deposit method are described. Direct and indirect evidence is presented that the ionization effect is due to the radiation which emerges from the arterial blood of the arm. Considerable variations of the dose of the active deposit of radium do not influence the results obtained. Repeated measurements in eleven individuals with regular rhythm agreed within an average of two seconds. The variation never was more than three seconds except in two individuals in whom it amounted to four seconds and five seconds, respectively. Measurements can be repeated as early as three hours. The circulation times of fifty-three normal resting male individuals are presented. The arm to arm circulation time in normal resting individuals may vary between fourteen and twenty-four seconds when the active deposit is injected into the cubital vein of one arm and the onset of radiation from the arterial vessels of the other arm is detected. The arm to arm circulation time does not become more prolonged with advancing age as measured by the method described. There is no critical age beyond which the velocity of blood flow tends to diminish. The average arm to arm circulation time in fifty-three normal persons between the ages of fifteen and seventy-five was eighteen seconds. The average arm to arm circulation time when reduced to square meter of body surface was ten seconds in individuals between the ages of fifteen and twenty-nine, and eleven sec-

onds between the ages of thirty and seventy-five. A few measurements in children indicate that the velocity of the blood flow is somewhat rapid in childhood.

With a conspicuous increase in the pulse rate there is a slight but definite tendency toward an increased velocity of blood flow. A relatively low ventricular rate does not seem to lower the velocity of blood flow below that exhibited by individuals with higher ventricular rates. Normal variations in the blood pressure bear no relation to the normal variations in the velocity of blood flow.

Blumgart, Herrmann L., and Yens, Otto C.: Studies on the Velocity of Blood Flow: I. The Method Utilized. Jour. Clin. Inves., 1927, iv, 1.

The authors describe a method developed by them for measuring the flow of blood in the living human being. The method consists of the injection of the active deposit of radium at one point in the body and the detection of its time of arrival at another point. The use of the active deposit of radium, or Radium C, has yielded a method which fulfills the criteria set up by the authors for the development of the method. In the present article the authors describe the apparatus used for detecting the appearance of the radium salts in the circulating blood at remote points.

They point out that the advantages of this method are as follows: The volume of fluid injected is very small. The substance injected is nontoxic in the amounts utilized. The presence of extraordinary minute amounts of the substance can be detected with certainty. The radiations by traversing the tissues of the arm automatically indicate the time of arrival of the active deposit. No withdrawal of blood is necessary. The method is objective, requiring no cooperation on the part of the patient. The method gives a quantitative estimate of a fundamental aspect of the circulation.

Davies, H. Whitridge and Gilchrist, A. Rae: Observations upon the Circulation Rate in Man by the Ethyl Iodide Method. Quart. Jour. Med., 1927, xx, 245.

The authors studied the circulation rate in eighteen individuals with the ethyl iodide method of Henderson and Haggard with several minor modifications. It was found that ethyl iodide reacted with the rubber parts of the apparatus especially with the noncollapsible tubing leading to the respiratory valves. To avoid this rubber connections were reduced to a minimum and metal tubing coated with red lead was used instead. For the respiratory valve advocated by Henderson and Haggard the authors substituted the Lovin valve. They found that on using the former the condensation of moisture from the expired air caused the

apposing rubber surfaces to stick together with a consequent increase of resistance to expiration.

Instead of using an oil bath to keep the U tubes used in analysis at a uniform temperature, it was found that an electrically heated hot air oven with a thermostat control was more satisfactory.

The technic employed was similar to that advocated by the originators of the method.

The effect of ethyl iodide itself on the circulation was discussed. With repeated determinations in one day it was found that symptoms of iodism sometimes developed. The authors also noted an apparent but inconstant fall in the circulation rate after repeated determinations and they discussed the possible explanation for this. Prolonged rest is ruled out as heavy muscular work was performed by one subject between determinations. The possibility of an accumulation of unhydrolyzed ethyl iodide in the blood giving a high alveolar content and therefore a low circulation rate is also considered. Another explanation is the depressant effect that ethyl iodide may have on the cardiac muscle from its concentration in the coronaries.

No relationship between body weight, height or surface and the circulation rate could be established. The fall in circulation rate after several determinations hampered the experiments destined to show changes after muscular exertion. After exercise the metabolism seemed to reach the normal level before the circulation rate decreased to the preexercise level. This difference may be greater than is estimated since the authors considered the repeated determinations as depressant to the circulation. The authors state that changes in circulation rate due to posture cannot be too carefully controlled. The metabolism changes must be watched and it may be that an alveolar sample is difficult to obtain in the supine position. Metabolism was shown to produce definite changes in the blood flow; chilling of the subjects produced greater oxygen consumption with a smaller proportionate increase in circulation rate, a slight rise in temperature probably being accompanied by the opposite effect. Psychological factors are also stressed, as altering circulation rate. It is urged that in determinations of circulation rate the above factors of temperature, metabolism, posture and activity be carefully controlled.

Bourne, Geoffrey: An Attempt at the Clinical Classification of Premature Ventricular Beats. Quart. Jour. Med., 1927, xx, 219.

The author described a method whereby the rate of occurrence of ventricular premature beats were estimated over a considerable period of time and under differing circumstances in a group of normal and cardiac individuals. The string galvanometer with Cohn's electrodes was used. The abnormal deflections were counted and noted at intervals of five to thirty seconds, the total time of observation being perhaps thirty minutes.

Twenty-eight cases showing frequent ventricular premature beats were studied. Seven of these were apparently normal individuals. The remaining 21 were divided according to the type of cardiac lesion present: Rheumatic cases without failure, rheumatic cases with failure, syphilitic, arteriosclerotic without failure, and arteriosclerotic with failure. The effect of exercise, posture, amyl nitrite and atropine was studied in these various groups with reference to the occurrence of extrasystoles and changes in the heart rate. The exercise used varied with the patients. Stepping off and on a chair 18 inches high until dyspnea supervened was the usual type, though in severe failure raising the thorax from the horizontal to the upright position a varying number of times was substituted. It was found that little or no change in the number of extrasystoles occurred with exercise in any group except among the arteriosclerotic subjects, where a definite increase in extrasystoles was noted after exercise in 9 out of 11 cases. The author explains the difference in reaction betwen arteriosclerotic and rheumatic cases by the presence in the former of coronary disease producing local patches of anoxemia in the myocardium. The absence of any marked tendency to increased ectopic beats in cardiac failure, rheumatic in origin, precludes general myocardial damage as the cause of the extrasystoles.

The author determined the effect of posture on the occurrence of premature beats and found that the number increased with the patient erect. Two factors must be considered here: (1) the fall in systolic pressure and (2) the rise in cardiac rate which occurs when the erect posture is assumed. The first might be a factor in the occurrence; the second probably would not, as it is known that extrasystoles diminish with a rise in the cardiac rate. The fall in peripheral systolic pressure was considered inadequate to explain the increase in extrasystoles and the author concluded that a variation in vagus sympathetic balance might be responsible.

Amyl nitrite when inhaled seemed to effect the number of extrasystoles in much the same way as exercise; i.e., an increased number in the arteriosclerotic cases, and as no increase in the load on the circulation was present, the effect probably depended on the tachycardia produced.

Atropine sulphate, $\frac{1}{50}$ grain, was given subcutaneously when it was found that coincident with the initial fall in rate the number of ectopic beats also fell: When the heart rate later rose, the premature beats were further diminished in 7 out of 10 cases and if a direct action on cardiac muscle can be ruled out the author suggests that the diminution is probably due to gradual change in the vagus sympathetic balance, that occur rather than to actual vagal stimulation or vagal paralysis.

The theories of parasystole and reentry are discussed in the light of the author's findings. Parasystole as the mechanism is ruled out by the presence of an increased number of premature beats occurring after exertion in three cases of pulsus alternans where the refractory period

was increased. Evidence in 13 of the cases pointed to reentry as the mechanism. In these cases increase in extrasystoles occurred with deceleration after a tachycardia when they were absent.

Anderson, J. P.: Auricular Fibrillation Associated with Hyperthyroidism. Am. Jour. Med. Sc., 1927, clxxiii, 788.

The importance of recognizing the presence of auricular fibrillation in cases of hyperthyroidism has led the author to offer this report of 120 cases in which this condition has been studied with special reference to the response of certain therapeutic measures. The average age of this group is fifty-two years, only 3 being under forty years of age. In cases of auricular fibrillation associated with hyperthyroidism in which the former condition is of recent onset, the heart action usually becomes regular after thyroidectomy or even the use of quinidine will usually suffice to cause the restoration of the normal rhythm. In cases in which auricular fibrillation is of long standing and is associated with hyperthyroidism of recent onset, thyroidectomy is well borne, although the heart action is seldom restored to a normal rhythm; the heart rate can be controlled by digitalis and the condition of the patient will be much improved.

Cases of hyperthyroidism in which a grave degree of heart failure is present and in which a regime of absolute rest, digitalis and Lugol's solution does not suffice to clear up the condition of the heart are always desperate risks and a considerable mortality is inevitable. In these cases, however, the prognosis without operation is also hopeless and operation should be performed if there is the slightest hope of its being successful.

In all cases of hyperthyroidism, the preoperative use of digitalis and of Lugol's solution for at least a week prior to operation is advisable. It is of special importance that the operation be performed before the onset of fibrillation or of heart failure.

Fineberg, M. H.: Systolic Hypertension: Its Relationship to Atherosclerosis of the Aorta and Larger Arteries. Am. Jour. Med. Sc., 1927, clxxiii, 835.

The author has studied 237 consecutive cases of elevated blood pressure in the Montefiore Hospital. Of these 66, or 28 per cent had high systolic and relatively low diastolic pressures.

Patients with elevated systolic pressure and a relatively low diastolic pressure form a definite group characterized clinically by their relatively advanced age, by comparative infrequency of complaints directly referable to the hypertension, by generalized atherosclerosis with particular involvement of the aorta, by moderate cardiac hypertrophy in about half the cases and by the presence of systolic murmurs over the mitral or aortic areas or both. In general, they tend to run a benign and prolonged course.

At autopsy they show moderate cardiac hypertrophy, some degenerative changes of the heart muscle, atherosclerosis of the aorta and coronary arteries, kidneys which grossly appear finely granular with large scars and microscopically show arteriosclerosis, and generalized arteriosclerosis of the entire vascular system.

The etiology of this type of hypertension cannot be determined as yet, but the sclerosis of the aorta and larger vessels is probably a factor.

These cases run a course and have a prognosis different from those with diastolic hypertension, in addition to having distinct clinical and pathological characteristics, and should, therefore, be differentiated and labelled as systolic hypertension.

Garvin, John D.: Hypotension: Six Cases in One Family. Jour. Am. Med. Assn., 1927, lxxxviii, 1875.

The author reports a group of six cases of essential and incidental hypotension in one family, 5 of which are in one generation, 3 brothers and 2 sisters and the sixth a son and nephew. These 6 patients with low blood pressure are in excellent health, are active and vigorous. Most of them are robust and hyperesthenic and one is obese. The figures of blood pressure represent the highest reading in several examinations at intervals over a period of two years. In each case they were made at or about midday with the patient fully clothed and sitting erect. With the possible exception of the physician in the group, the family is one characterized by extreme activity, efficiency in hard work, splendid physique and is of a stock noteworthy of its longevity. There are absolutely no evidences of failing myocardia to which such pressure might be attributed. The author concludes that individual hypotension is of little or no clinical pathological significance except as a possible indicator of long life. Hypotension, like hypertension, may be hereditary.

Huber, Edward G.: Systolic Blood Pressures of Healthy Adults in Relation to the Body Weight. Jour. Am. Med. Assn., 1927, lxxxviii, 1554.

Data as to height, weight, age, chest measurements and systolic blood pressures were obtained from the physical examinations of 1332 healthy men who are residing temporarily in the Southeast States.

The percentages above and below normal weight and blood pressure for each individual were computed, Symond's table being used as a standard for the weight and Siler's table for blood pressure. What little statistical significance attached to the correlation coefficient is to a considerable extent due to the fact that while 49 per cent of those who are more than 10 per cent under weight have subnormal blood pressure, only 18 per cent of those over weight have hypernormal pressures. Classifying blood pressures into two classes, those over 140 and those under

110, it is shown that 22 per cent of the former are under weight and 14 per cent over weight. Those with hypotension are 53 per cent under weight and 6 per cent over weight.

Dickinson, W. Richards, Jr., and Strauss, Marjorie L.: Oxyhemoglobin Dissociation Curves of Whole Blood in Anemia. Jour. Clin. Inves., 1927, iv, 105.

The present investigation represents a study of oxyhemoglobin dissociation curves of the whole blood of several subjects with anemia primary and secondary at serum P_Hs of 7.24, 7.44 and 7.64. At the low P_H value all curves studied were close to curves of normal blood. At serum P_H 7.64 the anemia curves were definitely lower than the normal. Points on the curve of a patient with polycythemia vera showed no evidence of abnormality.

Symposium on Circulatory Failure and Its Treatment:

Eberts, E. M.: 1. Circulatory Failure in Hemorrhage and Shock. Page 637.

Campbell, D. G.: 2. Circulatory Failure in Acute Infectious Diseases: Typhoid, Diphtheria, Scarlet Fever and Measles. Page 639.

Moffatt, C. F.: 3. Circulatory Failure in Acute and Chronic Cardiac Diseases: Myocarditis, Valvular Disease and Auricular Fibrillation. Page 643.

Meakins, J. C.: 4. Circulatory Failure in Chronic Intoxications and Vascular Disturbances; Hyperthyroidism, Chronic Anemia, Chronic Nephritis, Diabetes, Hypertension. Page 647.

Canadian Med. Jour., 1927, xvii, pages as above.

These four papers present clearly the principal features of circulatory failure in relation to the conditions described. An important feature of the group is the treatment of circulatory failure under these conditions. They form a valuable contribution to this subject and should be of general interest.

Meakins, Jonathan: Distribution of Jaundice in Circulatory Failure. Jour. Clin. Inves., 1927, iv, 135.

The appearance of primary pigmentation of the skin and viscera is a relatively common occurrence in severe circulatory failure. The author reports six cases in which the distribution of this pigmentation was localized to the upper part of the body. In all of the cases there was pronounced anasarca extending up to approximately the level of the ribs. The hands and lower forearms were usually without pigmentation, al-

though it was often present to some extent above the elbows. In those cases where an autopsy was procured, the endothelium of all the arteries and veins was deeply stained with bile pigment. This was followed into the smallest vessels possible.

The author discusses the probable cause of jaundice occurring in circulatory failure. He states that with our present knowledge, an adequate explanation is not clear.

Leas, R. D.: Vital Capacity: A Study of the Effect of Breathing Dry Air. Arch. Int. Med., 1927, xxxix, 475.

The author observed, by chance, that when a patient with cardiac decompensation was asked to inspire through a jar of calcium chloride for a five minute period, that the patient expressed his gratitude for the procedure because he felt so much better and could breathe more easily than before. The author has studied, therefore, a number of patients with asthmatic, cardiac and renal diseases and a few with pulmonary infiltration, to see the effect of dry air in extracting the moisture from the bronchial tree. The second series of 100 patients, normal as to heart and lungs, served as a control. The method consisted simply of taking the vital capacity on the Sanborn-Benedict metabolimeter before and after the patient breathed through a jar containing anhydrous calcium chloride. The author reports in this study the effect on vital capacity of breathing dry air. In the 100 control patients the average increase of vital capacity was 12.5 c.c. or 0.3 per cent.

The number of patients with cardiac decompensation showed an average increase of 190 c.c. or 11.4 per cent. In patients with cardiac compensation there was an average increase of only 35 c.c. or 1.3 per cent.

The author concludes that breathing dry air extracts enough of the moisture to increase temporarily the vital capacity in the majority of patients with bronchial edema; with this there is a decrease in the lung volume and in the number of râles. The patients described a sense of subjective relief. If the vital capacity is reduced, however, because of bronchial obstruction other than moisture, interstitial pulmonary edema or a rigid lung due to stasis, breathing dry air causes no change.

Alexander, H. L., Luten, Drew and Kountz, W. B.: Effects on the Heart of Long Standing Bronchial Asthma. Jour. Am. Med. Assn., 1927, lxxxviii, 882.

The criteria of true bronchial asthma were established in fifty patients in whom the condition had been evident for at least five consecutive years. The average duration of asthma was ten years. With one exception emphysema was present in all cases.

An examination of the heart was made in each of these patients. Three were found definitely injured but in two of these the cardiac disease

antedated the onset of the asthma. The third patient was seventy-eight years of age and had auricular fibrillation.

There were four patients in whom there were some suggestions of cardiac impairment but in none of these was there sufficient evidence to establish myocardial disease. The impression is gained that as a rule the heart remains singularly free from injury after continuous bronchial asthma despite the attendant emphysema.

It is suggested that the increased intrathoracic pressure which occurs during an asthmatic paroxysm may impede the return of the venous blood and that the work of the heart thereby actually may become diminished.

Kahn, Morris H.: The Electrocardiogram in Bronchial Asthma. Am. Jour. Med. Sc., 1927, clxxiii, 555.

In the present study the author analyzes the electrocardiograms of a series of cases in order to ascertain the effects of chronic emphysema and bronchial asthma upon the right ventricle. Of 50 cases of bronchial asthma and emphysema 10 showed electrocardiographic evidence of right ventricular preponderance.

The remaining cases showed electrocardiographically no preponderance and left ventricular preponderance in about equal numbers. Among these a large proportion of cases showed hypertension and aortic atheroma, factors which influenced the hypertrophy of the left ventricle to a degree sufficient to mass the evidence of electrocardiographical evidence of right ventricular hypertrophy.

Corwin, Jean and Herrick, W. W.: Relation of Hypertensive Toxemia of Pregnancy to Chronic Cardiovascular Disease. Jour. Am. Med. Assn., 1927, lxxxviii, 457.

A study of 165 cases of the subacute or hypertensive type of toxemia of pregnancy both during pregnancy and in a follow-up clinic, has brought to light a striking relationship between this type of toxic disturbance and chronic cardiovascular disease. In the cases thus observed 122 exhibited cardiac hypertrophy, sclerosis of the brachial and radial arteries, vascular retinal changes and persistent hypertension after a period of from six months to six years postpartum. Of these 37 per cent showed persistent hypertension.

Of 52 cases in one or more pregnancies subsequent to the one first attended by this type of toxemia, 50 showed hypertension in the subsequent pregnancies. In 21 the blood pressure in the subsequent pregnancies showed higher figures. In 16 the level reached was about the same, while in only 6 did the pressure tend to decrease with subsequent pregnancies.

Patients manifesting this type of disturbance should be observed over a series of years for evidence of cardiovascular disease. Patients with

cardiovascular disease should be safeguarded by a special medical care during pregnancy and should be discouraged from often repeated attempts at child-bearing.

Hyman, Albert S.: The "Doctor's Heart." Jour. Am. Med. Assn., 1927, lxxxviii, 712.

For those who support the idea of a clinical entity in the "Doctor's Heart" syndrome, the obituary columns of the large medical journals prove to be a source of confirmation. The author, therefore, has selected at random from personal files one hundred cases of physicians who have presented themselves for cardiovascular study. All of the physicians examined were in active urban practice.

In this group of physicians with suspected or actual cardiovascular disease, a high incidence of extrasystoles was noted. A great increase in blood pressure was not found. The types of heart disease discovered did not differ in any way from that found in other groups within the community.

While it is true that cardiovascular disease is the greatest cause of death among physicians, the belief that there is a clinical entity known as the "Doctor's Heart" is without foundation.

Robey, Wm. H., Freeman, Louis M.: The Effects of Tonsillectomy on the Acute Attack or Recurrence of Rheumatic Fever. Boston Med. Surg. Jour., 1927, cxcvi, 595.

The authors investigated in this study 454 public hospital patients out of a possible group of 910 who had been discharged with a diagnosis of rheumatic fever or chorea. In this group were included a few cases of repeated attacks of tonsillitis and rheumatic heart disease. Any case not having a clear history was excluded. The statistical tables published show that in the 201 cases with tonsillectomy as compared with the 253 cases without tonsillectomy, the subsequent history as regards recurrence and subsequent attacks of rheumatism and chorea was about the same. In the group with tonsillectomy 31 per cent gave a history of no subsequent attacks. In the group without tonsillectomy 35 per cent or 160 cases had no history of subsequent attacks.

It is the authors' belief, however, that complete enucleation of the tonsils offers the best preventive of rheumatic fever and therefore of rheumatic heart disease. Incomplete tonsillectomy leaves the patient in as dangerous a situation as before and throws discredit upon the value of tonsillectomy as a preventive. Tonsil remnants are often as formidable as the original tonsil. Tonsillectomy is a major operation and should be performed only by persons duly qualified.

Tonsillectomies were performed in about 60 cases of acute rheumatic fever during the height of attack. None were operated upon until all

medical measures had proved to be useless. The length of time from admission to operation varied from five to eight weeks. Some of these cases did not have rheumatic heart disease, while others entered with it, the result of previous attacks of rheumatism.

From these 60 cases the authors feel that the tonsils were without question the cause of the acute condition and that by removing them they shortened the course of the disease and prevented further injury to the heart. They noted no ill effects from operating at this stage of the disease. The prompt subsidence of fever and joint symptoms following tonsillectomy in this group has encouraged them to resort to the operation as soon as sufficient study has shown that the tonsil is the portal of entry.

Cutler, Elliott C.: Summary of Experiences Up-to-date in the Surgical Treatment of Angina Pectoris. Am. Jour. Med. Sc., 1927, clxxiii, 615.

The author reviews the various operations that have been devised for the surgical relief of angina pectoris. He discusses briefly the explanation for the relief that may be obtained by each of these procedures. He concludes that those operations which divide the known sensory pathway in the sympathetic nervous system connecting the heart with the central nervous system gives a fairly high percentage of satisfactory results. The failure of any single procedure to alleviate pain in all cases leaves him with the definite impression that much more is yet to be learned. The fact that the division of a certain pathway does not eradicate pain in every case and the fact that so many varied procedures give relief at one time and again fail, arouses strongly the question as to what it is that results in the clinical picture of angina pectoris.

Oliver, Sir Thomas: Heart Disease and Pregnancy. Brit. Med. Jour., 1927, No. 3458, 709.

From the records of the Princess Mary Maternity Hospital for the last three years there were 38 patients admitted with organic heart disease. Thirteen suffered from mitral stenosis, 12 from mitral regurgitation and 6 from aortic regurgitation. In the cases tabulated as mitral regurgitation it is likely that stenosis was present as well. Four of the 38 patients died in the hospital. The author discusses the danger of pregnancy to a woman with a damaged heart. He points out that mitral stenosis is usually regarded as the most common to be met with in women and to be the lesion which plays such a harmful part in the later months of pregnancy. He feels that on account of the hypertrophy of the left ventricle in aortic incompetence that this type of heart lesion is less frequently associated with serious consequences. In those individuals with muscular incompetence, serious difficulties arise early in the course of

pregnancy due to the increased volume of blood and the lack of ability of the heart to meet these changes.

He points out the necessity for observing closely such patients with heart disease during the course of pregnancy. If signs of embarrassment occur, pregnancy should be terminated.

Friedlander, Alfred: Hypotension. Medicine, 1927, vi, 143.

In this extensive review of the subject, the author presents a discussion of our present knowledge of blood pressure in relation to clinical medicine. He takes up studies of the normal blood pressures at varying periods of life and under varying conditions of daily life. He proceeds then to describe and to discuss those conditions associated with hypotension. He also discusses the effect of certain drugs, mechanical factors and various tissue extracts on blood pressure and hypotension. The review is extensive, is up-to-date, and presents all the views that have been written on this important subject. Conclusions in regard to the various phases of the subject are very carefully drawn and represent a conservative opinion in each instance.

Steinfield, Edward and Jacobs, Maurice S.: A Study of the Toxic Filtrates of Anhemolytic Streptococci, Recovered from Patients with Rheumatic Fever. Jour. Lab. and Clin. Med., 1927, xii, 850.

Berkefeld filtrates of cultures of anhemolytic streptococci isolated from the throats (particularly the tonsils) of three patients with rheumatic fever were lethal for guinea pigs in doses of 2 to 4 c.c. (representing 1 to 2 c.c. of original culture fluid). This property was also noted in the cultures of anhemolytic streptococci isolated from the blood of a patient with subacute bacterial endocarditis. Two other strains isolated from patients with rheumatic fever and two from normal individuals did not produce toxic filtrates.

The action of the toxic filtrate was evidenced by a slowing of the heart rate in guinea pigs and death in one to two weeks with some strains and in one to nine days with other strains. Deterioration was noted after a number of transplants with a loss in lethal power. Aschoff nodules and arthritis were not produced in the experimental animals.

The toxic principle, when present, was relatively weak in view of the comparatively large doses which were used.

Wyckoff, John and Goldring William: Intravenous Injection of Ouabain in Man. Arch. Int. Med., 1927, xxxix, 488.

The authors have studied the effect of Ouabain when given intravenously for the relief of patients with cardiac failure or who were unable to tolerate other forms of digitalis by mouth or rectally.

The patients were admitted to the hospital and put to bed on a limited

fluid intake and a uniform diet. Daily observations were made as to the ventricular rate, pulse rate, weight, water intake and urine output. In all 28 patients with auricular fibrillation, 3 with regular sinus rhythm and one with auricular flutter received 248 injections of the drug.

None of the patients showed harmful effects. One hundred and sixty-three of these injections were followed by a definite cardiac effect. An initial effect was noted in from five to twenty minutes, and the maximal effect in from fifteen to fifty minutes. As a rule the larger the dose, the earlier the initial effect and the more delayed the maximal effect. A greater amount of Ouabain was necessary to reduce the ventricular rate in patients who had auricular fibrillation with elevation of temperature than in those without elevation of temperature. The variation in dosage was less when calculated on the basis of body weight than on the basis of the total dosage. The persistence of the action of the drug was variable in cases observed, but in all except three the persistence was never longer than five days.

It would seem that Ouabain if given in fractional doses may be administered with safety intravenously to patients with auricular fibrillation that have not received digitalis recently. When Ouabain is given to patients with regular sinus rhythm, greater care must be used. In these patients clinical improvement seems to be the only criterion for full therapeutic effect, and since moribund patients may not show clinical improvement, there is greater danger of overdosage.

Birkhaug, Konrad E.: Rheumatic Fever: Bacteriologic Studies of a Nonmethemoglobin-forming Streptococcus with Special Reference to Its Soluble Toxin Production. Jour. Infect. Dis., 1927, xl, 549.

A new species of a nonmethemoglobin-forming, inulin-fermenting, bile-insoluble, and toxigenic, gram-positive streptococcus, was regularly isolated from the tonsillar crypts, abscesses, and irregularly from blood cultures, heart vegetations, feces and urine, of persons stigmatized by rheumatic fever and its syndromes.

Culturally, toxigenically and serologically, the nonmethemoglobin-forming streptococci constitute a closely related group of micro-organisms, distinguishable biologically from the groups of Streptococcus viridans and Streptococcus hemolyticus.

In a study of the production of soluble toxins by streptococci isolated from rheumatic fever patients, it was found that among 98 strains of Streptococcus hemolyticus, no toxin was demonstrated, among 247 strains of Streptococcus viridans, 4.7 per cent were toxin producers, and among 68 strains of the nonmethemoglobin-forming streptococcus, 72 per cent were found to produce a soluble toxic filtrate, slightly weaker in potency than that produced by the Streptococcus scarlatinae and Streptococcus erysipelatis.

Normal persons without history of rheumatic fever, when injected intradermally with 0.1 c.c. of a 1 to 10 dilution of the toxic filtrate of the nonmethemoglobin-forming streptococcus, 18 per cent of adults and 11 per cent of children gave positive skin reactions measuring more than 1 cm. in diameter within twenty-four hours after the injection.

Among persons with definite history of rheumatic fever and its syndromes, when tested intradermally with 0.1 c.c. of a 1:100 dilution of the soluble toxic filtrate produced by the nonmethemoglobin-forming streptococcus, 56 per cent of adults and 76 per cent of children gave positive skin reactions, and when tested with 1:10 dilutions of the toxin, 67 per cent of adults and 85 per cent of children reacted positively with lesions measuring more than 1 cm. in diameter within twenty-four hours after the injection.

Intramuscular injections of increasing doses of the toxic filtrate in laboratory animals and in humans susceptible to the toxin produced a neutralizing antitoxin.

Injected intravenously and subcutaneously in rabbits the nonmethemoglobin-forming streptococcus invariably produced nonsuppurative polyarthritis, subacute bacterial endocarditis, myocarditis and epicarditis, with unique tendency to mitral stenosis, extensive mural vegetations, and occasionally myocardial degeneration, with nodular cellular arrangements of multinuclear forms, as well as polymorphonuclear and mononuclear cells.

Injection intraarticularly and intramuscularly of large doses of the soluble toxic filtrate of the nonmethemoglobin-forming streptococcus in the author who previously had given repeatedly a strong positive intradermal reaction with 0.1 c.c. of a 1:100 dilution of the toxin, produced a typical clinical picture of acute polyarthritis of the rheumatic type, which healed without suppuration or injury to the articular surfaces.

Birkhaug, Konrad E.: Bacteriologic Studies in Acute Rheumatic Fever with Reference to Soluble Toxin Production. Proc. Soc. Exp. Biol. & Med., 1927, xxiv, 541.

A comparative study was made of the toxin production of hemolytic and nonhemolytic methemoglobin-forming streptococci and of a third variety which was originally obtained from blood culture in a fatal case of rheumatic carditis. Subsequently, a similar organism was regularly obtained from various sources in rheumatic subjects. This third group of streptococci were anhemolytic, did not form methemoglobin, were bile-insoluble and did not ferment inulin and it was thought that this organism was the same as that previously described by Zangemeister, Mendelbaum, Rosenow and Small.

The author tested for toxin production by the intradermal injection of 1 c.c. of a 1:100 dilution of filtrate and regarded as positive those reac-

tions which resembled the Dick test in appearance and measured more than one cm. after twenty-four hours.

Ninety-eight strains of hemolytic streptococci and 247 strains of green streptococci isolated from normal and diseased tonsils were used as controls and it was found that only 4.7 per cent of the control strains produced a toxin as judged by the skin reaction. The 68 strains of anhemolytic nongreen streptococci obtained from rheumatic fever cases were tested for toxin production in normal and rheumatic subjects and a much larger number of positive skin tests were obtained. Of the normal group 18 per cent of adults and 11 per cent of children were positive while in the rheumatic group 56 per cent of adults and 76 per cent of children gave positive skin tests. In lower dilutions the percentage of positive tests was higher and the local reaction resembled in some instances erythema nodosum. Neutralization of the toxin was obtained by mixing one skin test dose with 0.01 c.c. of serum from actively immunized rabbits. The toxic substances could be inactivated by boiling for one hour but failed to be destroyed by exposure to sunlight at room temperature for three months.

Addition of 6 volumes of absolute alcohol removed the active toxic principle completely and a precipitate was obtained, readily soluble in normal saline.

Injection of living bacteria into a rabbit produced a nonsuppurative polyarthritis and a bacterial endocarditis, while injection of sterile filtrate produced a nonsuppurative polyarthritis and myocardial degeneration.

The author who reacted with a positive skin test to the toxin from the anhemolytic nongreen streptococcus injected himself intraarticularly with 1 c.c. of sterile filtrate and produced a general polyarthritis with many of systemic symptoms of rheumatic fever.

The number of rheumatic persons reacting positively to a toxin suggested an allergic basis for rheumatism.

Reid, Wm. D., Kenway, Florence L.: The Action of Tetraiodophenolphthalein on the Heart. Jour. Am. Med. Assn., 1927, lxxxviii, 540.

Involvement of the heart has been suspected in the reactions following the injection of tetraiodophenolphthalein. Thirteen patients were studied electrocardiographically for evidence of cardiac change. No alterations from the control electrocardiograms were consistently present.

It seems reasonable to conclude that the injection of tetraiodophenolphthalein does not have a significant effect on the heart.